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Object: Selection procedure for a n. 1 annual departmental (PRIN 2022) research grant entitled: " Study of the effects of new target therapies on T-cell features of patients with chronic lymphocytic leukemia " for the Scientific Disciplinary Group 06/MEDS-09 - Blood diseases, oncology and rheumatology - Scientific Director Prof. Marta Coscia

THE DIRECTOR OF THE DEPARTMENT

- Given article no. 22 of the Law no. 240 of 30 December 2010, on research grants;
- Given the Decree of the Ministry for Education, University and Research no. 102 of 9 March 2011;
- 1, which establishes the minimum gross annual amount for research grants;
- Given the Regulations for the Assignment of Research Grants (hereafter the Regulations) issued by Rectoral Decree no. 903 of 24 July 2013, latest amendments issued by Rectoral Decree no. 2021 of 18 December 2017, effective as of 3 January 2018;
- Given the Law 30 December 2010, n. 240 art. 24 amended by Law no. 79/2022;
- Having seen the Legislative Decree 29 December 2022 n. 198 relating to urgent provisions regarding legislative deadlines;
- Given Ministerial Decree 639 of 2 May 2024 containing the determination of the scientific-disciplinary groups and the related declarations, as well as the rationalization and updating of the scientific-disciplinary sectors and the attribution of the latter to the scientific-disciplinary groups, pursuant to 'art. 15, of law 30 December 2010 n. 240;
- Given the Rectoral Decree Rep.586/2024 Prot. 52490 of 31 May 2024 for the classification of professors and researchers in scientific-disciplinary groups and scientific-disciplinary sectors, pursuant to the Ministerial Decree. 2 May 2024, n. 639;
- Given the Legislative Decree 29 December 2022 n. 198 relating to urgent provisions regarding legislative deadlines;
- Having considered the extension of research grants until containing the extension to 31 December 2024, included in the Legislative Decree of 31 May 2024, n. 71
- Given the acceptance of the financing by Prof. Marta Coscia;
- Having considered the request for activation of n. 1 annual departmental research grant for a PRIN 2022 project presented by Prof. Marta Coscia entitled "Study of the effects of new target therapies on T-cell features of patients with chronic lymphocytic leukemia" for the Scientific Disciplinary Group 06/MEDS-09 - Blood diseases, oncology and rheumatology, Scientific Disciplinary Sector MEDS-09/B – Blood diseases;
- Given the resolution of the Council of the Department of Medicine and Surgery Rep. n. 175/2024 which approves the activation of a selection for the assignment of





a of n. 1 departmental research grant for a PRIN 2022 project presented by Prof. Marta Coscia entitled “ Study of the effects of new target therapies on T-cell features of patients with chronic lymphocytic leukemia” in Area 06 - Medical Sciences, Disciplinary Scientific 06/MEDS-09 - Blood diseases, oncology and rheumatology, Scientific Disciplinary Sector MEDS-09/B – Blood diseases lasting 1 year, under the guidance of the Research Manager Prof. Marta Coscia;

- Financial availability for the PRIN 2022 project has been ascertained Prof.ssa Marta Coscia - CUP D53D23014180006;
- Ascertained that the amount of the grant referred to in this announcement finds financial coverage and accounting regularity of the expenditure of an amount equal to € 19,456.00 = gross recipient and € 23,999.62 = gross University for one year, which weighs on the project PRIN 2022 Prof. Marta Coscia - CUP D53D23014180006

DECREES

Art. 1 - Object

A selection procedure by titles, publications and interview for a research grant no. 1 annual departmental report (PRIN 2022) the academic recruitment sector the in Area 06 - Medical Sciences, Disciplinary Scientific 06/MEDS-09 - Blood diseases, oncology and rheumatology, Scientific Disciplinary Sector MEDS-09/B – Blood diseases lasting 1 year in the Department of Medicine and Surgery.

Research Title: “Study of the effects of new target therapies on T-cell features of patients with chronic lymphocytic leukemia”.

Research Project:

“In chronic lymphocytic leukemia (CLL), the efficacy of T cells engineered to express a chimeric antigen receptor (CAR T)-cell treatment has so far revealed suboptimal, due to a number of factors, including patient’s T-cell features of exhaustion and terminal differentiation. CLL is an exceptional model to investigate mechanisms affecting CAR-T cell functionality, as CD19 CAR-T cell therapy is effective only in a minority of patients. Despite the progress obtained in the treatment thanks to the introduction of targeted therapies, CLL remains an incurable disease, whereby CAR T cells might represent a valuable option, if an improvement of functionality could be achieved. It is interesting to note that the treatment with novel targeted drugs appears to empirically improve the generation and efficacy of CD19-directed CAR-T cells from patients with CLL. Based on this existing background, the objective of our research project is to assess the immunomodulatory effect exerted by targeted drug treatment in patients with CLL, particularly focusing on T-cell features that are known to affect the CAR T-cell generation and efficacy.

Patients with CLL requiring treatment and who are planning to start therapy with BTK inhibitors (ibrutinib, acalabrutinib o zanubrutinib) or the BCL2 antagonist venetoclax, will be enrolled into the study. At least 12 patients for each treatment cohort will be enrolled. Blood will be withdrawn before treatment initiation, and after 6 and 12 months of treatment. At each timepoint, the purified T lymphocytes isolated from the peripheral blood samples of patients undergoing treatment with targeted agents will be profiled in terms of T-cell enrichment; percentage and absolute numbers of CD4 and CD8 T cells, and $\gamma\delta$ T cells; percentage and absolute numbers of Tregs; percentage of Th subsets;



percentage of naïve, central memory, stem cell memory, effector memory and terminally-differentiated T cells; percentage of T cells expressing activation markers (i.e. CD69, CD25, HLADR) and immune checkpoint molecules (PD-1, CTLA-4, TIGIT, Tim-3, LAG3). At the same timepoints, in collaboration with the Department of Molecular Biotechnology and Health Sciences of the University of Torino, CAR T cells directed against the CD19 antigen will be generated from T lymphocytes purified from the peripheral blood of the same CLL patients. The efficiency of CAR T-cell generation and their immunophenotypic and functional characteristics will be correlated with the characteristics of the pre-manufacturing T-cell source and with their modulation during treatment. The research fellow will primarily be dedicated to the extensive immunophenotypic characterization of T lymphocytes and its correlation with the characteristics of CAR-T cells.

This research will be carried out in the Department of Medicine and Surgery of the University of Insubria

Research Coordinator: Professor Marta Coscia.

Art. 2 – General requirements

All those who have obtained

- Specialist degree in Medicine and Surgery (46/S), lasting no less than 5 years, obtained according to the educational system in force prior to the Ministerial Decree. n. 509/1999 and subsequent amendments or Biological Sciences (6/S) or Medical Biotechnologies (9/S),
- Master's Degree in Medicine and Surgery (LM-41) or Biological Sciences (class LM-6), or in Medical Biotechnology (class LM-9) obtained pursuant to the Ministerial Decree. 270/2004

A similar academic qualification obtained abroad and recognized as equivalent to the Italian qualification by the competent academic authorities, and who have an appropriate scientific-professional curriculum to carry out research activities established by this competition notice can participate in this public selection.

The following constitute **preferential requirements**:

- excellent knowledge of the English language;
- documented experience in setting up cell cultures and flow cytometry techniques.

Candidates must have no criminal record.

Applicants in possession of degrees earned abroad, who have not obtained the declaration of equivalence, must enclose in the application form a translation into Italian and a declaration of value of the foreign degree by a qualified Italian Diplomatic or Consular Representative in the country of origin, according to the Laws in force on the subject. The degree earned abroad can be declared admissible, by the Judging Commission, only for purposes related to the selection.



Qualifications must be possessed on the date of closure established for the presentation of the application form.

Those who have already received grants according to law n. 240 of 30 December 2010 for more than 6 years, except for the period corresponding to a PhD without scholarship within the maximum limit of the legal duration of the related course, cannot participate in the selection. For the purpose of the duration of the grant, periods spent on maternity or sick leave are not relevant according to the current regulations.

Art. 3 – Incompatibility

Personnel employed in Universities and in other public institutions can participate in the selection procedure, as of article no. 22, paragraph 1 of the Law no. 240 of 30 December 2010, but must resign should they obtain the research grant.

Civil Servants from different institutions from those mentioned in the paragraph above can receive the research grant, but must be placed on unpaid leave for the duration of the research grant.

The research grant is not compatible with enrolment in undergraduate courses, graduate courses, PhD courses with scholarship or medical specialization schools, in Italy or abroad, and with enrolment in other Schools/Courses which require mandatory attendance and prevent carrying out the activities established in the contract.

Relatives and in-laws within and including the fourth degree of a professor who is a member of the Department or the Structure which requested the Research Grant, or of the Rector, Director General or of a member of the University's Board of Directors cannot participate in the selection procedure for the assignment of a research grant.

The research grant cannot be cumulated with other kinds of granted scholarships, with the exception of those awarded by national or foreign institutions to aid, with periods of study abroad, the education of the Research Fellows. The research grant cannot be cumulated with subordinate work, with contracts of collaboration or with income deriving from freelance activities conducted in a continuous way.

Art. 4 – Application and deadlines

The application for participation in the selection, as well as qualifications held, the documents and publications voted helpful for the competition **must be submitted, under penalty of exclusion, via computer**, using the computer application dedicated to page: <https://pica.cineca.it/uninsubria/dmc2024-adr004>

The computer application will necessarily require the possession of an e-mail address in order to perform the self-registration system. The candidate will have to enter all data required for the production of the application and attach the documents in PDF format. You can attach a maximum of n. 30 documents for publications and n. 30 documents for other qualifications to evaluate, and maximum 30 Mb.

The application form must be completed in all its parts, as indicated in the electronic procedure, and must include:

- A scientific and professional CV
- A copy of a valid ID card



No other forms of submission of applications or useful documentation for participation in the procedure are allowed.

Within the application deadline, the procedure can be saved in draft mode. The date of electronic submission of the request for participation in the selection is certified by the computer system through an automatic receipt, which will be automatically sent via e-mail.

At the end of the submission period, the system will no longer allow access and submission of electronic forms.

Every application will be assigned an identification number, which, together with the selection procedure code in the application information, must be specified for any subsequent communication.

The process of compiling and sending electronic application must be complete **no later than 11:59 PM November, 14 2024.**

The submission of the application form must be completed and concluded as follows:

- **Sign your document on the ConFirma server**
To digitally sign the document, you must have specific hardware which is compatible with the ConFirma service (for example, smart card or USB device with a digital certificate of subscription issued by an accredited certifying body). After signing, it will be possible to download the signed PDF file
- **Digitally sign the document on your electronic device**
To digitally sign the document, you must have specific hardware (for example, smart card or USB device with a digital certificate of subscription issued by an accredited certifying body) and a digital signature software with which you may create, starting from the PDF file of the document downloaded from this site, a signed pdf.p7m file. The pdf.p7m file must be uploaded again to the website
- **Sign the application (no digital signature)**
If you can't sign the document digitally as specified in the other sections, you need to download the PDF file of the application, print it, sign it, scan it in a PDF file and upload it again to the website.

ATTENTION: a copy of a valid ID card must be attached as the last page of the scanned PDF, after the application form pages (this step can be skipped if a copy of the document was uploaded as an attachment of the application form).

Applications without the candidate's signature will be declared inadmissible.

Foreign nationals who reside in Italy can take advantage of the self-certification above, when substantiating states, facts and personal qualities certifiable by public or private Italian entities (article no. 3 of the Decree of the President of the Republic no. 445 / 2000).

Foreign nationals who do not reside in Italy cannot use in any way the institution of self-certification (article no. 3 of the Decree of the President of the Republic no. 445/2000). Qualifications, certifications and publications which do not comply to the abovementioned indications will not be taken into account. In the application of the rules on self-certification, the University will verify the accuracy of the substitutive declarations and self-certifications pursuant to the Decree of the President of the Republic no. 445/2000.



Only the documents received by the final deadline indicated in the call will be considered valid. The addition of qualifications earned or presented after the expiration date of the deadline of the call will not be admissible to the selection procedure.

Reference to documents and publications previously submitted for participation in other selection procedures in this or other Administrations is not allowed.

Candidates must provide at their expense to the restitution of qualifications and publications sent to participate in the selection procedure, prior to agreements with the Research and Internationalization Office of the University of Insubria.

Art. 5 - Information on the implementation of legislation on the prevention of corruption

The University, in implementation of the legislation on the subject, adopted its three-year plan for the prevention of corruption and appointed the Head of the Prevention of Corruption.

The three-year plan is published on the institutional website at <http://www4.uninsubria.it/on-line/home/naviga-per-tema/amministrazione-trasparente/articolo4719.html>

Any reports can be sent to: anticorruzione@uninsubria.it

Art. 6 – Selection Procedure

The selection procedure is carried out through a comparative evaluation of the CVs of the candidates who have applied, on the basis of their qualifications and publications and an interview.

The evaluation of qualifications and publications will be held electronically on **November, 19 2024 at 01:00 pm**.

The interview will take place on **December 2024, 3 at 09:00 am** and the location will be communicated to candidates who are eligible following the evaluation of qualifications and publications via the e-mail address indicated in the application form.

The ranking relating to the score received for the evaluation of qualifications and publications will be published on the University website with the value of notifying interested parties.

Furthermore, candidates will receive a communication regarding the outcome of the evaluation of qualifications and publications via e-mail to the address indicated in the application

For the evaluation of candidates, the Commission has 70 points of which:

- for titles and publications: up to a maximum of 30 points;
- for interview: up to a maximum of 40 points;

Candidates who have achieved an overall score of no less than **18/70** in the evaluation of their qualifications and publications will be admitted to the interview.



Access to the interview is open to candidates whose qualifications and publications have been assessed and who have therefore not been excluded for the reasons set out in the art. 7.

To be included in the final ranking, after the interview, candidates must have achieved an overall score of no less than **42/70**.

QUALIFICATIONS

- 1) Specialist degree in Medicine and Surgery (46/S), lasting no less than 5 years, or Biological Sciences (6/S) or Medical Biotechnologies (9/S) obtained according to the educational system in force prior to the Ministerial Decree. n. 509/1999 and subsequent amendments;

Master's Degree in Medicine and Surgery (LM-41) or Biological Sciences (class LM-6), or in Medical Biotechnology (class LM-9) obtained pursuant to the Ministerial Decree. 270/2004

maximum 15/70

and in particular:

- score 110/110 with honors 15.0 points;
- score from 105 to 110 points 10.0;
- score from 99 to 104 points 7.0;
- score less than 99 points 5.0;

- 2) - excellent knowledge of the English language;
 - documented experience in setting up cell cultures and flow cytometry techniques;maximum 10/70

PUBLICATIONS

- 3) - scientific publications maximum 5/70

INTERVIEW (UP TO 40 POINTS)

Evaluation of knowledge of the topic of the research grant and more. maximum 40/70

At the end of the work, the Commission will announce the result of the selection and compile a merit ranking.

The final list is approved by the Director of the Department and will be posted on the University's official online Board and on the website as notification to those concerned. The merit ranking will be used in the case of withdrawal or termination of the research grant; in this case, the position will be offered to the next candidate in the ranking list, provided that the period proposed for the contract is not less than one year.

Art. 7 – Exclusion

Candidates are admitted conditionally.

The following imply exclusion from the procedure:



- 1) submission of the application after the expiration date of the call;
- 2) failure to sign the application form;
- 3) lack of participation requirements;
- 4) existence of situations of incompatibility.

Exclusion is provided for with a motivated decision of the Director of the Department and will be communicated to the candidate using the e-mail address provided in the application.

Art. 8 – Withdrawal

Should candidates decide to withdraw from the procedure, they should send the withdrawal form via email to the address indicated above in article no. 4 of this call.

Art. 9 – Collaboration contract

The selection result is communicated to the recipient of the research grant, who will have to sign the private-law contract within a specified period, otherwise they will forfeit. This fixed-term contract does not represent in any way a permanent contract of employment and does not give right to be admitted to permanent positions within the University. The University provides equal opportunities to men and women.

The grant implies carrying out the activities briefly mentioned below at the Department of Medicine and Surgery of the University of Insubria and under the supervision of the Research Coordinator Prof. Marta Coscia within the research program: “Study of the effects of new target therapies on T-cell features of patients with chronic lymphocytic leukemia”.

The conditions are indicated by the contract and governed by the Regulations.

The grant is awarded for a period of 1 year in accordance with current legislation.

The contracts referred to in Article no. 24 of Law no. 240/2010, also with different universities and research institutions, as described in paragraph no. 1 of article no. 3 of this call, may in no case exceed twelve years, including non-consecutive ones. For the purposes of the abovementioned contract, periods spent on maternity or sick leave, in accordance with the current regulations, are not considered.

For non-EU citizens, the grant will start when they have obtained the residence permit for scientific research, and from the actual beginning of the research activity.

Art. 10 - Recruitment and HRS4R

The recruitment of fixed-term researchers (or Established Researchers, using the European definition) will conform to the European Charter for Researchers (ECR), the Code of Conduct for the Recruitment of Researchers (CCRR) and the Code of Ethics, code of conduct and principles of research integrity of the University of Insubria, which provide the general framework for the guidelines and requisites for the roles, responsibilities and rights of these positions, thus guaranteeing that selections procedures are open, transparent and meritocratic.



The University of Insubria received the European Quality Award “HRS4R - Human Resources Strategy for Researchers” in February 2019: such certification recognizes organizations their efforts to implement the Charter and Code in their policies and practice, and identifies the universities and institutions which create and promote a stimulating and encouraging research environment.

Art. 11 – Remuneration

The amount for the two-year period of the research grant is equal to € 19.456,00= inclusive of taxes and which must be paid by the recipient.

The University will provide medical insurance and third-party civil liability.

The amount is tax free according to article no. 4 of the Law no. 476 of 13/08/1984 and is subject, on social security matters, to the regulations according to article no. 2, paragraph 26 and following amendments and additions, of the Law no. 335 of 8/08/1995. The grant will be paid in monthly instalments.

Art. 12 - Suspension of the contract for maternity and sick leave

The research activity is suspended for maternity leave.

To such a case there apply the provisions of the Decree of the Ministry of Labor and Social Policies of 12/07/2007, published in the Official Journal no. 247 of 23/10/07. Sick leave is regulated by article no. 1, paragraph 788 of the Law no. 296 of 27/12/2006 and following amendments and additions.

During the period of mandatory maternity leave, the amount paid by the National Institute for Social Security (INPS), according to article no. 5 of the abovementioned Decree of 12/07/2007, will be integrated by the University to match the total amount of the research grant.

The period of mandatory maternity leave must be made up for after the natural expiration of the contract, as provided by the law, upon decision of the Director of the Department.

Art. 13 – Termination by the recipient of the research grant

The recipient has the right to terminate the relationship, by notifying the Director of the Department with a notice of at least thirty days.

Failure to notify will entail withholding remuneration for a sum related to the period of failed notice.

Art. 14 – Termination of the contract

Should the Research Fellow not continue the activities provided for in the research program without justification or in case of serious and repeated shortcomings, the contract may be terminated upon reasoned request of the research Coordinator, authorized by a resolution of the Department's Board.

The contract is automatically terminated, without prior notice, in the following cases:

- undue failure to commence or undue delay of the activity;
- undue suspension of the activity for a period exceeding 15 days;
- serious infringement of incompatibility, according to article no. 7 of the Regulations.



- negative assessment of the research activity on the part of the Department's Board.

The termination provisions are ordered by the Director of the Department.

Art. 15 – PhD and Master's Degrees

The recipient of the research grant can attend, also in excess and without scholarship, PhD courses, provided that they pass admission tests.

The participation of the recipients of research grants in Master's degrees is incompatible.

Art. 16 – Administrative proceedings

According to Law n. 241 dated 7/08/1990 Dr Roberto Battisti - Administration Office, Department of Medicine and Surgery, the University of Insubria Via Guicciardini 9, 21100 Varese, Italy e-mail: segreteria.dimit@uninsubria.it. in charge of the administrative proceedings

Art. 17 – Processing of personal data

In applying the Legislative Decree no. 196/2003, the University undertakes to respect the confidential nature of the information provided by the candidate. All data provided will be handled only for purposes connected to the selection procedure and to the management of the collaboration relationship, with respect to the current regulations as provided for in the attached document.

Art. 18 - Final regulations and publication

For matters not provided for in this call, please refer to the applicable laws and regulations on the subject.

This call will be published on the University's official online Board and on the "Calls" page of the University, of the Ministry of Education, University and Research and of the European Union websites.

Varese, *October 29 2024*

THE DIRECTOR OF THE DEPARTMENT

Prof. Luigina Guasti

Digitally signed

DATE OF PUBLICATION ON THE OFFICIAL ONLINE BOARD on October, 30th 2024

EXPIRATION DATE OF THE TERMS on November, 14th 2024

Responsabile del Procedimento Amministrativo (L. 241/1990): Dr. Roberto Battisti
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