



ID code: A009

The integral version is available at the following link:

<https://www.unimi.it/it/ricerca/fare-ricerca-da-noi/assegni-di-ricerca/bandi-assegni-di-ricerca>

THE ENGLISH LANGUAGE TRANSLATION DOES NOT HAVE LEGAL VALUE IN ITSELF, AND THUS DOES NOT SUPERSEDE THE ITALIAN VERSION OF THE CALL ANNOUNCEMENT (BANDO).

PUBLIC COMPETITION FOR 24 MONTHS FOR 1 TYPE A FELLOWSHIP FOR COLLABORATION TO RESEARCH ACTIVITIES IN THE SCIENTIFIC AREA OF MEDICAL SCIENCES.

ART. 1 - COMPETITION NOTICE

According to art. 2 of Regulations, this University has launched a competition by qualifications and interview to award 1 two years type A FELLOWSHIP, for a collaboration to research activities for the scientific area of Medical Sciences, restricted to doctorate graduates or graduated holding a diploma in the specialty health area. for collaboration to research activities.

ART. 2 - REQUIREMENTS

All graduates who have an appropriate scientific-professional curriculum to carry out research activities established by this competition notice can participate in this public selection.

completed by appropriate scientific production, unless otherwise specified, is preferential requirement for admission according to this competition notice.

Candidates must meet the following requirements:

- a. Absence of criminal record;
- b. Master's Degree or equivalent, from an Italian or foreign university.
- c. PhD or equivalent qualification obtained abroad or medical specialization degree
- d. Expertise in research area:

Expertise in the analysis of biomarker expression on histopathological samples by immunohistochemistry and immunofluorescence imaging. Expertise in in vitro and in vivo models of tumorigenesis and functional phenotype studies. Expertise in molecular biology and cell culturing. Expertise in bioinformatic analyses.

- e. Knowledge of language: English

Qualifications must be owned on the date of expiry established for the presentation of the application form.

Applicants in possession of degrees obtained abroad, who have not the declaration of equivalence, will have to enclose in the application form a translation into Italian or into English of the foreign degree, (Degree with marks earned in each examination and PHD degree), completed by a self-certification related to the correspondence to the original of the translation itself.



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The degree earned abroad can be declared admissible, by the Judging Commission, only for purposes related to the selection.

The following qualifications will be evaluated for purposes related to the competition:

- a. PhD thesis or equivalent qualification earned abroad or Medical Specialization thesis degree;
- b. Any Master's degree;
- c. Scientific-professional curriculum based on proven experience for research activity already carried out at public and private bodies with contracts, fellowships or appointments, both in Italy and abroad;

ART. 3 - CANDIDATES LIST AND CURRICULA PUBLICATION

In application of obligations of transparency as from D.lgs. 14/03/2013 n. 33 this competition notice, the list of candidates with their curriculum vitae and the result of each selection will be published on the web site http://www.unimi.it/ricerca/assegnj_ricerca/69536.htm.

ART. 4 - APPLICATION

Application forms in plain paper must be written according to the form at the following link: <https://www.unimi.it/it/ricerca/fare-ricerca-da-noi/assegni-di-ricerca> TYPE A section, and include name, surname, place and date of birth, address, telephone number, competition notice information. Application forms must be submitted online, at the following email address: unimi@postecert.it, within **December 19, 2024 at 11.59 pm (Italian time)**. The application form and any other enclosures requiring the candidate's signature. The message should state in the object field:

“Pec: Domanda concorso Assegno di Ricerca Prof. PECE SALVATORE, code ID A009”

Application forms not signed or incomplete or sent after the deadline established will not be admitted.

The application form must enclose:

- a. Degree with final mark;
- b. Phd degree / specialization degree (pdf file);
- c. Scientific qualifications, diplomas, scholarships, attendance of post-graduate courses;
- d. Up to 6 publications in PDF format (scientific publications in qualified reviews, with a list of them and a justification for their choice);
- e. Curriculum of scientific activities (use the template at: <https://www.unimi.it/it/ricerca/fare-ricerca-da-noi/assegni-di-ricerca> , TYPE A section);
- f. Research project related to the title of this call.

Documents above mentioned can be presented as follows:



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Academic and professional qualifications can be self-certificated, according to DPR 28/12/2000 n. 445. The other qualifications which require evaluation, publications included, can be presented in original or copy.

ART. 5 - CURRICULUM PRESENTATION

Candidates, by the same time of presentation of the application form, must scan and send to the e-mail address curriculum.assegni@unimi.it a copy of the curriculum vitae in pdf with the ID code with date according to the form at the following link: <https://www.unimi.it/it/ricerca/fare-ricerca-da-noi/assegni-di-ricerca> - [TYPE A section](#).

ART. 6 - RESEARCH ACTIVITIES

The Fellowship implies carrying out the activities briefly mentioned below at Dipartimento di Oncologia ed Emato-Oncologia dell'Università degli Studi di Milano and under the supervision of Prof. PECE SALVATORE within the research programme "***Deconvolution of NUMB-deficient bladder cancer heterogeneity to identify prognostic and therapeutic biomarkers for personalized patient management.***", of the following research program and its specific aims:

BACKGROUND AND RATIONALE

The goal of this proposal is to identify therapeutic vulnerabilities and predictive/prognostic biomarkers to advance a framework for precision oncology for the bladder cancer disease by generating a high-resolution picture of the at the cellular level of the molecular and phenotypic intra- and extra-tumor heterogeneity of bladder cancer. Indeed, despite ranking among the most common neoplasms in industrialized countries, with high incidence and prevalence rates and considerably high socioeconomical costs, bladder cancer remains surprisingly understudied and underfunded, with very limited progress towards improving its prognosis, treatment and patients' quality of life.

Our proposal builds on the recent discovery that loss of the tumor suppressor, NUMB, is a hallmark of biological and clinical aggressiveness in bladder cancer (Tucci F.A. et al. Tucci F.A. et al. *BioRxiv* doi.org/10.1101/2024.08.27.609735). Our aim is to develop a multi-tier approach based on the combination of global and single-cell transcriptomic profiling and spatial in situ multiplexed imaging to decipher the intricacies of the NUMB-deficient bladder cancer at the cellular level and highlight the heterogeneity of the NUMB-deficient bladder cancer ecosystem.

HYPOTHESES, AND SPECIFIC AIMS

We hypothesize that:

- a) NUMB-deficient bladder tumorigenesis is a disease continuum driven by subclones with stemness/plasticity traits, which display unique propensity to muscle-invasion progression, informing disease outcome.
- b) The intrinsic aggressiveness of these subclones depends on their unique repertoire of overexpressed pathways connected with RHOA/ROCK/YAP signaling to the actin cytoskeleton,



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involving a feed-forward regulatory loop influencing extracellular matrix remodeling and stiffness.

c) NUMB loss in the primary tumor associates with an impaired innate and adaptive TME immune response, which might directly depend on the secretion of anti-inflammatory mediators by NUMB-deficient bladder cancer cells or, not necessarily in a mutually exclusive fashion, on indirect regulation of the qualitative/quantitative tumor microenvironment immune infiltrate composition, possibly depending on variations of the matrix stiffness, according to the emerging field of “mechano-immunology”.

EXPERIMENTAL PLAN

By the execution of this experimental plan, we expect to identify tumor autonomous mechanisms and specific cellular states potentially associated with muscle invasion and immune response modulation, based on the spatial reconstruction of subclonal intratumor and extra-tumor heterogeneity. Specifically, we expect to identify a “transcriptomic signature of plasticity/stemness/invasiveness”, likely reflecting specific cellular states/subclones, and a “spatial inflammatory/immune signature”, with clinical potential for the management of the NMIBC disease. Towards these goals, we will leverage a variety of preclinical mouse and human BCa models and real-life patient samples in a sequential workflow from high-dimensional single-cell and spatial in situ analyses to high-resolution in vitro and in vivo functional validation studies.

The research activities are reported here:

1. Analysis of bladder tumor tissue by immunohistochemistry, multiplexed immunofluorescence and spatial in situ transcriptomics for resolution of tumor heterogeneity.;
2. Bioinformatics analyses for the identification of molecular signatures.;
3. Use of in vitro and in vivo model systems for the functional validation of actionable targets.;
4. Molecular biology and cell culture techniques.

ART. 7 - INCOMPATIBILITIES

For requisitions of admission and incompatibilities please see art. 6 and 8 of Regulations at the link:

<https://www.unimi.it/it/ateneo/normative/regolamenti/regolamento-gli-assegni-di-ricerca>

ART. 8 - FELLOWSHIP AND INSURANCE

The Fellowship’s yearly gross amount is of Euro 21.000,00. The amount is tax free according to art. 4 Legge 13 August 1984 n. 476 and subject, for what concerns welfare regulations, to regulations as from art. 2 paragraphs 26 and following Legge 8 August 1995 n. 335.

University will provide, for the period of the contract of collaboration to research, private insurance cover, with a public liability insurance and industrial accident insurance in favour of the fellow and within carrying out of research activities. The amount of the premium for insurance



against industrial accidents is subtracted each year from the remuneration for the fellow.

ART. 9 - PAYMENT AND SUPERVISION

The amount is paid in postponed monthly instalments. The Fellows' duties, established by the individual contract, are performed under the supervision of the Professor coordinator who will verify the activity carried out according to art. 8 paragraph 5 of Regulations.

ART. 10 - SELECTION PROCESS

Application forms will be examined by a judging Commission, specifically appointed by the Rector. The evaluation criteria for qualifications and scientific-professional curriculum are the following:

- curriculum vitae et studiorum;
- attendance of master degree;
- specialization degrees;
- attendance of post-graduate courses;
- PhD thesis
- research activity in Italy;
- research activity abroad;
- *fellowships*, scientific-professional contracts and appointments;
- participation in scientific congresses;
- up to 6 publications in PDF format (scientific publications in qualified reviews, with a list of them and a justification for their choice);
- monographic publications and chapters in books with explanation, for each publication, of the rationale behind the choice;
- patents;
- identity card scanned;
- other qualifications;

Evaluation criteria for research projects are the following:

- relevance of the project to the subject suggested by the Department;
- originality and feasibility of the research suggested, updating of the project, appropriate bibliographic reference;

The assessment of qualifications and of the research project takes place before the interviews and the results of assessments will be let known, for each subject, by publication in the web



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site: <https://www.unimi.it/en/research/doing-research-us/research-fellowships>. The date and place of the interviews will be communicated to the candidates at least 15 days in advance, by publication in the web site mentioned above with reference to the subject concerned.

For the evaluation of the candidates, the commission has 100 points, 65 of which are to be attributed overall to the qualifications, the scientific-professional curriculum of the candidate and the research project and the remaining 35 points to be reserved for the interview. Candidates who earn more than 32,5 points in the qualifications and in the project are admitted to the interview.

The interview aims to assess the contents of the project proposed by the candidate and scientific competences developed. The sub commission can use up to 35 points and the interview is overcome if the candidate earns more than 17,5 points. Candidates admitted to the interview, resident abroad, can do a telematics interview by means of procedures that guarantee their identification.

In case of equal result in the same subject, the fellowship will be awarded to the youngest candidate.

Art. 11 - Winner not compliant with competition notice and regulations

Winners of fellowships who do not comply what established by this competition notice and Regulations lose the right to the fellowship upon Rector's act by previous written communication.

ART. 12 - PLACE AVAILABLE IN CASE OF LOSS OF RIGHT OR RENOUNCE BY WINNER

In case of loss of the right or lack of stipulation within the deadline established or possible renounce by the winners, fellowships are made available to the candidates usefully placed in the ranking that, according to what established by Regulations, is valid up to ninety days from the approval of acts.

ART. 13 - PERSON IN CHARGE OF THIS COMPETITION

According to Legge 7 August 1990, n. 241 Mrs Anna Tavano at Direzione Trattamenti Economici e Lavoro Autonomo - Via S. Antonio n. 12, Milano is in charge of the competition as from this competition notice.

For more information please contact the Ufficio Contratti di Formazione e Ricerca at Direzione Trattamenti Economici e Lavoro Autonomo - e-mail: assegni.postdoc@unimi.it.

For what is not established by this competition notice, please see laws in Regulations and laws in force on the subject.

According to DL 196/2003 and according to the General Data Protection Regulation (GDPR) EU 2016/679 and to Regulations on the protection of personal data of the University of Milan



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University will commit itself to respect all confidential information provided by the candidate: “all information provided will be handled only for aims connected to the selection and to the stipulation and management of relationship with University”.

Full information is available at: <https://www.unimi.it/it/ateneo/normative/privacy> of the University website.

THE RECTOR
Marina Brambilla