HUMANITAS UNIVERSITY

Selection procedure for a Type B Research Fellowship in Life Sciences in compliance with art. 22 of law 240/2010 – Ref. D.R. 112/2016

Humanitas University invites applications for a position as Research Fellow in Life Sciences.

Research Program Title	Exploring the transcriptional and epigenetic bases of human neutrophil and monocyte dysfunction in aging
Research supervisor - Tutor	Prof. Gioacchino Natoli
Scientific Area	05- Biological science
Gross amount of the fellowship	35.000 Euro
Duration of the fellowship	36 months
Objectives of the research	Genomic dataset analyses

The work place is in Rozzano - Milano.

A brief description of the: project, activities to be carried out, mandatory requirements to take part into the selection process, information on the application procedure and on the selection criteria are presented in the following.

RESEARCH PROJECT:

The increased burden of infectious diseases in the elderly has a complex and multifactorial origin and can be ascribed both to primary alterations in the immune system and to changes in lifestyle, including wrong alimentary habits and use of medications. While changes in adaptive immunity in the elderly have been extensively documented, the role of impaired innate immunity has been overlooked and probably underestimated. Data accumulated in the last years indicate that, with age, innate immune cells develop functional abnormalities whose characterization and mechanistic understanding is still largely incomplete. Neutrophils are an essential first line of defense against a broad spectrum of microbes that cause severe infections in the elderly (pneumonia, urinary tract infections and periodontal diseases), while monocytes are recruited to sites of infection as a second line of broad-acting defense and give rise to inflammatory macrophages.

This project aims at a systematic characterization and mechanistic understanding of changes in neutrophil and monocyte function in normal aged individuals (>65 yo). The project consists of two main arms, namely i) the characterization of the functional properties of highly purified human neutrophils and monocytes from aged individuals vs. young adults, and ii) a systems-level analysis of the transcriptional and chromatin mediated changes occurring with age.

The specific working hypothesis at the basis of this project is that the functional changes in neutrophil and monocyte function that occur with age are associated with the cell-intrinsic activation (or repression) of distinct gene regulatory networks enforced by specific transcription

factors and chromatin modifications, thus resulting in different transcriptional outputs and functional prerogatives. Sequence-specific transcription factors are recruited to genomic regions that control transcription of adjacent or distant genes (promoters and enhancers). The differential usage of the enormous repertoire of available genomic regulatory elements in different cells or functional states in fact reflects the identity of the transcription factors selectively active in those different cell types or conditions. When recruited to specific genomic sites involved in regulation of gene expression, transcription factors recruit enzymes such as histone acetyltransferases and chromatin remodellers that locally alter chromatin thus supporting their own activity. Therefore most chromatin modifications represent footprints of transcription factor binding and a differential marking or accessibility of genomic regions in different conditions can be used to infer (using specific computational tools) and then experimentally validate, those transcription factors that control condition-specific usage of the genomic repertoire of regulatory elements, thus eventually leading to distinct gene expression programs and function. This epigenomic footprinting approach we have already successfully used in the past, will be used here to infer the regulatory circuits controlling the distinct functional properties of neutrophils and monocytes of young adult vs. old humans. Linking these circuits to known upstream regulators will allow formulating specific hypotheses (such as the differential activity of signalling pathways or availability of metabolic mediators) that will be directly tested to eventually determine which mechanisms are responsible for (or contribute to) functional deterioration of innate immune cells in the elderly. These data will provide a rigorous mechanistic and molecular framework for the specific functional properties of neutrophils, as well as monocytes, in normal aged individuals and may be useful to hypothesize corrective interventions to recondition such cells and restore their normal functionality.

ACTIVITIES TO BE CARRIED OUT:

The successful candidate will mainly carry out the exploration of the transcriptional and epigenetic bases of human neutrophil and monocyte dysfunction in aging.

MANDATORY REQUIREMENTS:

In order to be considered for the post candidates must hold either a PhD or a diploma of medical specialist in scientific areas consistent with the one specified in the notice or an equivalent qualification obtained in Italy or abroad.

SELECTION PROCESS:

Applications should be written on plain paper according to the application form attached (ALLEGATO A) to the Rectoral Decree n. 112/2016 (available at page http://www.hunimed.eu/it/lavora-con-noi/) and must be produced, under penalty of exclusion, within twenty (20) days from the day of the publication of the notice. If the specified deadline falls on a public holiday, the deadline is the next working day.

The application form, duly signed, under penalty of exclusion, can be sent in one of the following ways:

1. via certified email (PEC) by sending the application and all relevant documents, in PDF format, to hunimed@pec.it (quoting in the subject: "*Research Project title as stated in the table above*" with the indication scientific area relevant for this post. Please note that certified email can only be received by other PEC; therefore will not be considered valid, the application sent by an e-mail address that is not certified as PEC.

2. Either via registered letter with acknowledgment of receipt, courier or hand-delivered to the Rector of the University Humanitas, "Segreteria del Rettorato della Università Humanitas" via Manzoni No. 113-20089 Rozzano (MI), by the deadline mention above specifying on the envelope the "Research Project title as stated in the table above", the name and address of the candidate.

Applications must include:

1. a curriculum vitae dated and signed, containing the description of any professional or research experience (including publications and participation at conferences);

2. a copy of a valid document of identity or, for Non-EU citizens, a copy of applicant's passport.

For EU citizens or equivalent, that which has been declared in the application form (ALLEGATO A) assumes substitute value of certifications according to DPR 445/2000;

Applications can also include:

3. a dated and signed list of the titles presented;

4. a dated and signed list of the publication presented;

All the titles and publications presented together with the application can be produced on plain paper together with a declaration made according to the model attached (ALLEGATO B) to the Rectoral Decree n. 112/2016 (available at page http://www.hunimed.eu/it/lavora-con-noi/)

As part of the selection process, a Selection Committee will evaluate the curriculum, titles and publications presented by the candidate.

SELECTION CRITERIA:

The Candidate should have a previous expertise in the analysis of RNA-seq and ChIP-seq data sets documented by published papers and an excellent knowledge of the English language.

FURTHER INFORMATION:

For more details on the selection process please refer to the Rectoral Decree n. 112/2016 (http://www.hunimed.eu/it/lavora-con-noi/) or send an inquiry to ufficiodocenti@hunimed.eu or contact the following number +39 02.8224.5642.