DC12: Targeted demethylation of ncRNAs involved in 3D chromatin hubs in cancer

Host institution: Istituto Italiano di Tecnologia, Centre for Human Technologies, Genova, Italy

Supervisor: Dr. Dafne Campigli Di Giammartino

Co-Supervisors: Dr. Francesco Nicassio, Istituto Italiano di Tecnologia (Academic); Prof. Federico Forneris, Instituto Universitatrio di Studi Superiori di Pavia (Academic); Prof. Niall Barron, National Institute for Bioprocessing Research and Training (Industrial).

Project description: 3D chromatin architecture plays a crucial role in facilitating interactions between regulatory elements and gene loci, thereby influencing cellular function and identity. Long non-coding RNAs (lncRNAs) are key mediators in this spatial organization and recent advances suggest that epitranscript modifications such as N6-methyladenosine (m6A) on ncRNAs can modulate their function and stability, impacting chromatin dynamics. Building on these insights, and on the preliminary data produced in-house, this PhD project will focus on the implementation of a dCas13 protein fused with an m6A eraser to reverse m6A modification on previously selected ncRNAs that were found to be enriched in highly connected chromatin regions, with the final goal of uncovering novel molecular mechanisms that influence chromatin architecture and gene expression regulation in cancer stem cells.

The project will be structured in three phases: 1) Establish a dox-inducible system for expression of dCas13-m6Aeraser fused protein in two patient-derived glioma stem cell lines 2) Validate the efficient m6A removal from candidate ncRNAs 3) Evaluate the effects on local/global 3D chromatin interactivity (Hi-C, HiChIP, 4C-seq), and correlate with changes in gene expression (RT-qPCR and RNA-seq) and the epigenetic landscape (H3K27ac/H3K4me3/ H3K27me ChIP-seq or Cut&Tag).

The overreaching aim will be to understand the functional role of ncRNAs and their epitranscript modifications in shaping 3D chromatin architecture and regulating gene expression, leading to potential discoveries of actionable targets that could have therapeutic relevance for tumor treatment.

Host laboratory: Research activities in the group of Dr Campigli Di Giammartino aim at understanding how non-coding elements (such as enhancers and non-coding RNAs) and their epigenetic/epitranscriptomic modifications regulate 3D genome architecture, gene expression and cell identity. To address this question, we use cutting-edge chromatin conformation assays (e.g.Hi-C, Hi-ChIP, Micro-C) in conjunction with other -omics techniques (e.g. ChIPseq, RNA-seq etc.) and in combination with CRISPR-based genetic and epigenetic engineering tools in mouse stem cells as well as in human tumor stem cells.

The laboratory is an integral part of the IIT RNA Flagship program, it collaborates closely with laboratories of the Human Technopole Functional Genomics unit and is an active member of the international FANTOM6 project on non-coding RNAs and chromatin regulation, providing the lab with a lively global research community.

Secondments: This project is carried out in strong collaboration with the following groups, and visits to their laboratories are expected during the project. A willingness to travel and spend time abroad is therefore essential:

- Prof. Barbara Uszczynska-Ratajczak, Institute of Bioorganic Chemistry, Polish Academy of Sciences, Poland;
- Prof. Niall Barron, National Institute for Bioprocessing Research and Training, Ireland

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the European Research Executive Agency. Neither the European Union nor the granting authority can be held responsible for them.

Funded by the European Union

Eligibility conditions:

- Master's degree in Biology, Molecular Biology, Biotechnology or related program
- Applicants must be doctoral candidates, i.e. not already in possession of a doctoral degree.
- Mobility rule: researchers must not have resided or carried out their main activity in the country of the recruiting beneficiary for more than 12 months in the 36 months immediately before their recruitment date.

Required Skills:

- Research experience (e.g. through Master thesis work or research internships) in cellular and molecular biology techniques are required. Familiarity with the non-coding RNA fileld, CRISPR technologies and/or previous experience in producing NGS data (such as ChIP-seq, RNA-seq) will be considered a strong advantage.
- Proficiency in the English language is required, as well as good communication skills, both oral and written. Successful candidates will need to provide an English test (e.g. IELTS, TOEFL, Cambridge English). You may be exempt if you are a national of a majority native-English speaking country, or have qualifications / degree that has been taught and assessed in English. The supervisor can also confirm during the interview that a candidate has the required level of English.

Enquiries

For general information about the INT2ACT Doctoral Network visit the visit the project website (www.int2act.eu) or send an email to int2act@gmail.com.
For additional information on this project please contact Dr. Dafne Campigli Di Giammartino (dafne.campigli@iit.it).

How to apply

To learn more about the application process, visit the INT2ACT recruitment web page (https://int2act.eu/open-positions/).

Required documents:

1. Statement of interest (limit of 2,500 characters) explaining why you wish to be considered for the fellowship and which qualities and experience you will bring to the role.
2. Curriculum vitae et studiorum.
3. A certificate of University examinations taken (with marks).
4. A final degree certificate translated in English. If, at the time of application, candidates should not be yet in possession of a degree certificate, they can submit it at the time of the examination.

All documents must be merged into a single PDF file, in the order listed above.
A limited number of applicants will be invited for an interview and will be required to provide contact information of up to two contact person for reference letters.

Application deadline

The closing date for applications is **January 31 2026.**