DC10: Tools to target epitranscriptomic modifications on transgenic mRNA

Host institution: National Institute for Bioprocessing Research and Training, Dublin, Ireland

Supervisor: Prof. Niall Barron

Co-supervisors: Dr. Nga Lao, National Institute for Bioprocessing Research and Training (Industrial); Dr. Jessica Ferti, baseclick GmbH (Industrial); Prof. Rory Johnson, University College Dublin (Academic).

Project description: There is significant interest in the use of mRNAs as vaccines since the development of the novel Covid vaccines during the pandemic, but also as potential therapeutics in their own right, or as a means to engineer adoptive cell therapies. This project will create biotherapeutic production cell lines and tools to program the host cell to engineer in or out specific mRNA methylation events in a targeted manner in order to improve the yield of biotherapeutics from these cell lines. However mRNA is often short-lived in cells and therefore modifications, such as methylation, which increase half-life and/or increase translation could be very beneficial. We propose to **[1]** Selectively delete or overexpress genes involved in RNA methylation in CHO, HEK293 and other target cells; **[2]** Create transgenic cell lines stably expressing either a programmable RNA methyltransferase or demethylase; **[3]** Examine the recombinant protein (e.g. monoclonal antibody) and viral gene therapy vector (e.g. lentivirus) productivity from these novel transgenic host cell lines

Host laboratory: Biological medicines based on proteins, nucleic acids or even living cells are difficult to manufacture efficiently, safely and economically. Our research focuses on understanding and improving the cell systems used to create these therapies with a particular emphasis on the cellular molecular mechanisms involved. We apply advanced omics technologies to identify the genes and pathways that contribute to cellular phenotypes relevant to, for example, producing monoclonal antibodies or other therapeutic proteins in Chinese Hamster Ovary (CHO) cells.
In this way we try to develop genetic engineering strategies to enhance the ability of the host cell line to make these products more efficiently. These strategies include manipulating the expression of specific endogenous genes (including non-coding RNAs, not just protein-encoding genes) in the host cell line, introducing exogenous sequences into the host or modifying the genome directly – ideally in a highly targeted manner.
We apply similar strategies to enhancing the manufacturing platforms for viral gene therapy vectors (e.g. AAV or lentivirus) including HEK293 or Sf9. Gene therapies present unique challenges in terms of their production including low yield, high variability and a dependency on large-scale transient transfection of multiple expression plasmids. Modified cell therapies (e.g. CAR-T) are another exciting new modality demonstrating some spectacular clinical results but which, particularly in the autologous setting, are exceptionally challenging to manufacture. The CEG lab at NIBRT are interested is various aspects of creating these cell therapies including more efficient gene delivery approaches and the use of modified RNA to enhance the expression of the relevant transgenes.

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.

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Secondments: This project will be in collaboration with the following groups, and visits to their laboratories are expected during the project:

- Prof. Rory Johnson, University College Dublin, Ireland;
- Dr. Jessica Fertl, baseclick GmbH, Germany.

Eligibility conditions:

- BSc or Master's degree in Biology, Biotechnology or related field.
- 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. Experience in RNA biology will be 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 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. Carlo Vascotto (carlo.vascotto@uniud.it).

How to apply

To learn more about the application process, visit the INT2ACT recruitment web page (www./int2act/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.**