DC7: Study of human immune reaction to lung transplantation in a xenograft mouse model

Host institution: Miltenyi Biotec

Country: Germany

Supervisory team: Dr Eleni Papanikolaou (Miltenyi Biotec), Prof. Laurens Ceulemans (KU Leuven

Project description:

Engraftment of human CD34 cells into immunocompromised NSG mice is an established xenograft model to study human immunity, but interestingly, it has never been tested in the context of lung transplantation. In LifeLUNG, this model will be investigated by DC7 with the potential to identify novel targets related to lung transplant rejection, for gene editing during EVLP. They will use the capabilities of the MACSima™ and RNASky™ platforms to study the homing of human CD34 cells in the mouse lung, CD34 gene expression during their active regeneration and the interplay between the human immune system and mouse lung.

The objectives are: 1. Assessment of the regenerative capacity of engineered and non-engineered CD34 cells from the same donor after ex vivo (in vitro) genetic engineering in NSG mice using the MICS technology. 2. In vivo targeting of CD34 cells with anti CD133-pseudotyped LNPs following humanization on NSG mice. 3. Identify potential targets for gene editing to reduce risk of LTx rejection.

A successful project will result in: Generation of a protein atlas involved in homing of human CD34 cells in the mouse lung. Identification of genes expressed during active regeneration of CD34 cells in the mouse lung, advancing the knowledge around transplantation beyond the state of the art in the xenogenic setting. Addressing the potential interplay between the human immune system developed in the mouse with the mouse lung in the xenogenic transplantation setting.

Your role:

- While obtaining your PhD, you will have the opportunity to join a dynamic team and develop solutions to improve gene therapy for hemoglobinopathies towards clinical translation.
- You will intensively work with human and murine hemopoietic stem cells that you genetically correct with several genetic tools (LNPs, electroporation, viral vectors etc). You will then characterize these modified cells for functionality in vitro using a wide panel of tools and technologies as well as in vivo.
- As you love to explore new approaches and develop new solutions, you will apply a broad spectrum of different methods including, primary hemopoietic cell culture and differentiation, culture of stable cells lines, immunophenotyping assays based on fluorescent cytometric cell analysis, etc. You will also help develop and use automated screening assays to accelerate your work.
- Molecular biology and gene therapy are your favorite topics and you are keen to apply your skills and knowledge of both topics synergistically.
- This position offers you the unique opportunity to obtain your PhD while developing new technologies and gaining scientific insights in a very dynamic field and gives you the chance to learn how ideas will translate into practice and become a therapy concept.

Essential requirements of a successful candidate

- You must not have resided or carried out your main activity (work, studies, etc.) in Germany for more than 12 months in the 36 months immediately before the start of your PhD. Compulsory national service, short stays such as holidays, and time spent as part of a procedure for obtaining refugee status under the Geneva Convention are not taken into account.
- You must not be in possession of a doctoral degree.
- You hold a Master's degree (no PhD) in biomedical sciences, molecular biology, bioengineering, biotechnology, pharmacy or a related field, or an MD.
- You are passionate about life sciences and biomedicine, and want to achieve a PhD degree on the topic described in the description above

- You are experienced with molecular biology technics and with (primary) cell culture and capable of working with novel devices (e.g. Flow cytometers)
- Preferably, you are familiar with functional testing of primary human cells and highly interested in performing in vivo experiments using mouse models.
- You are ambitious, well organized, and have excellent communication skills.
- You are proficient in English both spoken and written
- You have a solutions-oriented mindset that thrives in a multidisciplinary team
- You have the ability to work independently and have a critical mindset.
- You are an enthusiastic and motivated person, eager to participate in network-wide training events, international travel, and public awareness activities.
- Willingness to travel
- You are a team player and interested to work in interdisciplinary teams

Skills and expertise that are viewed as an asset:

- Knowledge and experience in gene therapies, translational research, immunology, and regenerative medicine
- Experience in advanced microscopy and mass spectrometry
- Experience in GLP, animal and lung models
- Experience in omics methods, data analysis, and interpretation

What we offer:

- A modern workplace and exciting opportunities in the development of technologies with a secure future
- Cross-border intercultural cooperation and short communication channels
- A collegial corporate culture and flexible working hours enable time management on your own terms
- Personalized employee development program: specialist and personal training courses provided by our own Miltenyi University training platform
- Diverse corporate benefits with regard to employee health, sport, and staff events

Who we are:

- Our innovative solutions for biomedical research have made us a global leader in the development of treatments for severe diseases
- Currently we have more than 2000 employees in our interdisciplinary teams working on technologies with a secure future
- Our international, multicultural, owner-led team can be found in our headquarters in Bergisch Gladbach, near Cologne, and in our 25 subsidiary companies around the world
- Progress is the driver of our research and we celebrate our success together. This philosophy means that, each and every day, we are getting closer to realizing our corporate vision of developing treatments for severe diseases.

Additional information:
Enrolment in Doctoral School: KUL Doctoral school of Biomedical Sciences, Faculty of Medicine.

Application procedure:
If you have the skills and qualifications for this position, please use the link to send us your details (application letter, curriculum vitae, references and certificates) or send an email to elenip@miltenyi.com (subject: LifeLUNG). The deadline for applications is September 28th, 23.59pm CET.

The position as PhD fellow is full time and lasts 3 years.