IBEC-BST INTERNATIONAL PhD PROGRAMME

Position

1. Project Title/ Job Position title:
   Spatial multi-omics on iPSC-derived CAR-NK effector cells to identify gene modifications with improved anti-tumor performance

2. Research project/ Research Group description:

Chimeric antigen receptor (CAR) therapy has led to remarkable remission rates in patients with previously untreatable blood cancers, solidifying CAR therapy as a game-changer in oncology. However, as of today, there are no FDA/EMA-approved CAR therapies for solid tumors. This is mainly due to the reduced efficacy of those cells in the solid tumor microenvironment because of the hostile cues that they receive. Recently, Natural Killer (NK) cells have raised as one of the most promising cell types to be engineered against solid tumors (1). The main goal of this work is evaluating gene modifications in iPSC-derived CAR-NK-cells on tumor infiltration, cell fitness, and performance in the hostile tumor microenvironment, with the long-term goal to provide alternative options to improve current cell-based therapies for cancer.

iPSC are an attractive source of CAR-mediated immunotherapies as they can be genetically modified and clonally expanded producing homogeneous effector cells upon differentiation and eliminating the need for viral vector gene modifications (1). Genetically modified iPSC can be unlimitedly expanded, providing a reproducible research model and a suitable source of cell therapies (2). The iPSC-derived Advanced Therapies group at the BST will provide expertise in iPSC and NK therapies. We will utilize advanced spatial biology profiling techniques developed by the Spatial Biotechnology group (IBEC) to map cell distribution of CAR-NK-cells on the tumor microenvironment.

This project combines the unique strengths of both groups to develop a cutting-edge platform to identify gene modifications on iPSC-derived CAR-NK effector cells with improved anti-tumor performance in solid tumors. The work will validate a platform that could be easily adapted to other cell types and tumor models and provide fundamental insights into engineered NK cell biology, paving the way for novel cell-based therapeutic strategies against solid tumors.

1. *Li Y et al. Human iPSC-Derived Natural Killer Cells Engineered with Chimeric Antigen Receptors Enhance Anti-tumor Activity. Cell Stem Cell. 2018 Aug 2;23(2):181-192.e5.*
2. *Yamanaka S. Pluripotent Stem Cell-Based Cell Therapy-Promise and Challenges. Cell Stem Cell. 2020 Oct 1;27(4):523-531.*

3. Job position description:

This collaborative project offers a unique PhD training opportunity at the interface of cell-based therapies for cancer and advanced tissue imaging.

Main tasks and responsibilities:

- Perform gene modifications on iPSC cell lines with previously identified candidates that can potentially overcome the greatest challenges of (CAR-)NK cells to effectively exert anti-tumor activity in solid-tumors models.
- Differentiate iPSC into NK cells with and without CAR-expression, using the protocols optimized by the iPDA group at the BST.
- Develop heterogenous tumor models and sample processing protocols compatible with spatial biology technologies, and test (CAR-)NK cells in in vitro and in vivo tumor models.
- Implement pipelines for spatial tissue analysis.

Requirements for candidates:

Essential:

- BSc and MSc in biomedicine, biotechnology, or related fields.
- A strong commitment to scientific research and an excellent academic record.
- Good working knowledge of English.
- The candidates must not have held a PhD contract exceeding twelve months by the beginning of the fellowship in September 2025.
- Good skills in communication, teamwork, proactivity, commitment, integrity, time management, critical and analytical thinking, precision, and focus.
- Willingness to work in a highly multidisciplinary environment.

Advantageous:

- Experience programming and scripting in Python or R, and experience in image analysis.

Group Leader at IBEC

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4. Research Group: Spatial Biotechnology

Group Leader at SJD

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4. Research group: iPSC-derived Advanced Therapies