

## Challenge based learning (CBL)

### Industrial manufacturing of iPSC-derived tissue engineered products to treat macular degeneration

**Note for teachers:** A CBL user guide can be found at [www.jandeboerlab.com/TissueEngineering](http://www.jandeboerlab.com/TissueEngineering) with instructions and tips to run an effective CBL teaching session.

#### Background and vision

The last step in research and development of a tissue-engineered product (TEP), before it can be introduced in the market, is to set up an industrial manufacturing process. Manufacturing of TEPs follows a specific regulatory framework which focusses not on the efficacy of the product but rather on the technical requirements of the manufacturing process. The process needs to be described in meticulous detail. Because every successful research line in tissue engineering will eventually enter into this phase, our vision is that future tissue engineers should include the aspects of the product manufacturing process early in the exploration phase.

#### Motivation and stakeholders

Currently, there is a mismatch between the TEP production process in academic laboratories and manufacturing processes for clinical-grade products. Therefore, many TEP manufacturing processes are underdeveloped and suboptimal. In these cases, process scalability and reproducibility represent a major hurdle. To bring a TEP to market, engineers need to generate a detailed design of the manufacturing process. Modern process management strategies, including the quality-by-design concept, are increasingly used to set up manufacturing processes for TEPs in the clinic. Attempts to implement these strategies for TEP manufacturing should consider the needs, requirements and regulatory, financial and technical boundary conditions defined by stakeholders such as patients, surgeons, tissue and biomedical engineers, manufacturing engineers, chemical engineers, regulatory bodies, industrial engineers, and biotechnology engineers involved in the manufacturing of TEPs.

#### Problem definition

Macular degeneration is treated with iPSC-derived epithelial cells but in order to be used as a TEP, the process has to comply to the regulation of the Advanced Therapy Medicinal Products (ATMPs), Gene Therapy Medicinal Products (GTMPs) and Cell Therapy Medicinal Products (CTMPs). Hence, the process has to be described according to these regulations.

#### Challenge

To design an efficient and cost-effective TEP process following Quality by Design (QbD) methodology for the generation of a cell therapy medicinal product from iPSCs to treat and cure macular degeneration.

#### Learning framework

Reading the Product and Process Design chapter and related literature will help you to:

1. Understand the rules set out by the notified bodies on ATMPs.
2. Know the nomenclature of the process such as unit operations, process monitoring, and scalability.
3. Acknowledge the advantage of design requirements in the QbD methodology.
4. Comprehend the advantages of automation, single-use equipment, and improved mathematical process models involved in the manufacturing of ATMPs.

For a more focused examination of the challenge, read scientific literature and create a mind map to include information about the following:

5. The steps for current TEPs to comply with EMA regulations.
6. Cell culture systems used in TEP manufacturing.
7. Unit operations in the production of cells for macular degeneration treatment.
8. Aspects of the manufacturing process to be described according to the regulations.

#### End product

A three-minute video explaining the solution of your challenge. Please include your motivation and the steps to execute your solution.