Advanced
Organ bioengineering &
Therapeutics

Development of a Bioluminescent-joint-on-chip: A non-invasive platform for screening anti-osteoarthritic drugs

Background

Osteoarthritis (OA) is a joint disease affecting over 528 million people globally, and approximately 1.2 million people in the Netherlands. Characterized by synovial inflammation, cartilage degradation, and pathological changes in the underlying bone, OA presents a significant clinical challenge. Despite its widespread impact, effective treatments remain limited. This is largely due to heterogeneity within patient populations as a result of diverse clinical phenotypes and biomolecular endotypes (i.e., distinct pathological pathway signatures), which complicate the development of an universal therapy. Due to this, there is a need for individualized treatment approaches rather than the use of general pain and inflammation relieving medications.

Traditionally viewed as a “wear and tear” disease associated with aging, recent research shows that OA initiation and progression is closely linked to the immune system. Certain inflammatory pathways, have been identified as key drivers of OA, in specific patient subsets. These insights open up the possibility of tailoring therapies to interfere with these pathways. One promising approach to screen the effect of therapies on these pathways involves the use of reporter cell lines derived from joint tissues. These cell lines can be engineered to express key proteins associated with OA inflammatory pathways and used to develop and screen drugs targeting those proteins (Figure 1).

To facilitate drug screening, these reporter genes can be linked to luciferase enzymes, enabling real-time monitoring via bioluminescence imaging (BLI). Compared to fluorescence imaging, BLI offers several advantages: it is non-invasive, does not require sample fixation, avoids photobleaching, and supports in-situ, long-term tracking—making it especially useful for evaluating dynamic drug responses.

However, drug development also requires models that closely mimic the complexity of human joint tissues. Traditional 2D cell cultures fall short in replicating the intricacies of human tissues. Therefore, this project will utilize organ-on-chip (OoC) technology, which offers a more physiologically relevant platform for disease modelling and therapeutic screening.

In this assignment, you will contribute to the development of a simplified joint-on-chip model incorporating both osteochondral and synovial components. The model will integrate reporter cell lines of specific proteins involved in inflammatory pathways in OA, enabling the screening of candidate drugs that modulate key inflammatory pathways implicated in OA.

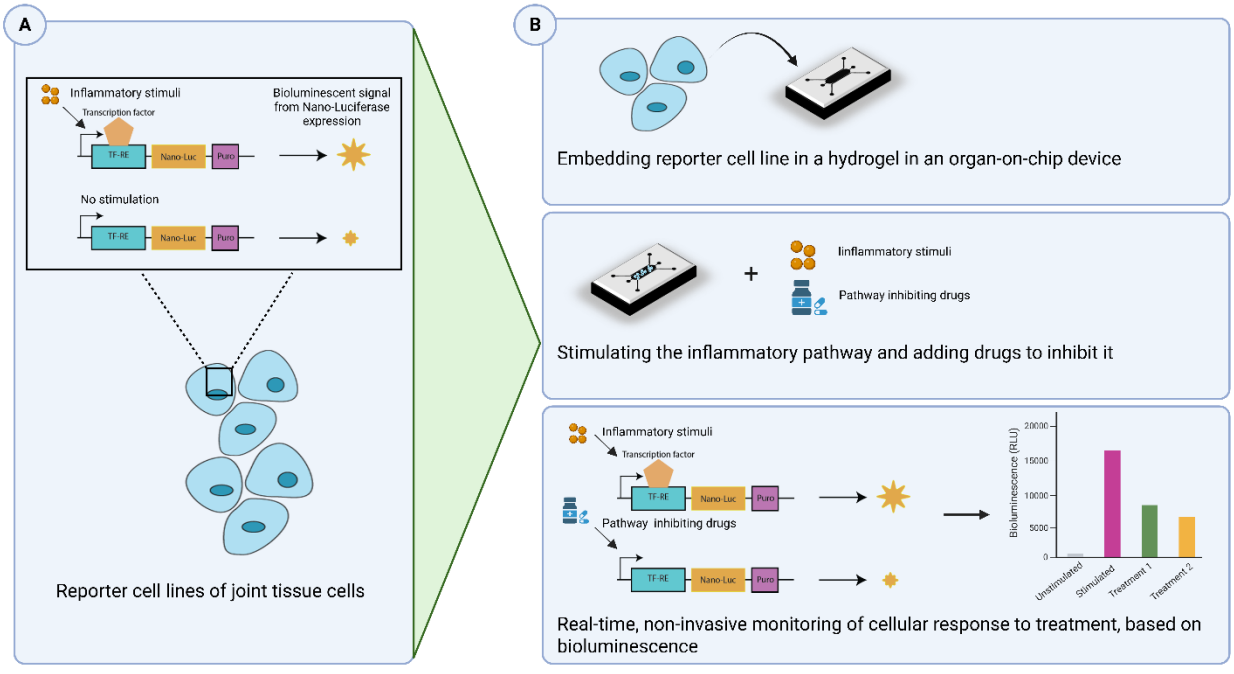

*Figure 1: Overview of the core concept of the project. **A**: Components and working of a reporter cell line; **B**: General workflow combining reporter cell line with organ-on-chip device.*

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Objectives of assignment:

Objective 1: Set up 2D reporter assays with synovial fibroblast and osteoblast reporter cell lines to screen pathway inhibiting drugs

Objective 2: Optimize hydrogels for synovial and osteoblast-on-chip units.

Objective 3: Transfer optimized assay from 2D wells plate system to organ-on-chip device to enable drug screening.

Skills to be acquired:

- Cell culture of synovial fibroblast and osteoblast reporter cell lines
- 2D assay development for drug screening
- Microfabrication of organ-on-chip using soft lithography with PDMS
- Flow driven microfluidics
- Work with hydrogels to construct tissue microarchitecture
- Confocal and fluorescence microscopy
- Bioluminescence readout on-chip (PEARL imager, bioluminescence microscope)

Supervisors:

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Supervisors: Dr. Liliana Moreira Teixeira (AOT), Prof. Marcel Karperien (DBE).