# Challenge based learning (CBL)

# The use of iPSCs to model SARS-Cov-2 infection in kidney organoids

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

**Background and vision**

Severe acute respiratory syndrome (SARS) is caused by a novel microorganism called coronavirus 2. The resulting coronavirus disease (COVID-19) is an infectious problem caused by the SARS-Cov-2 virus which has unleashed a pandemic never seen before. Over the past 3 years, this

disease caused seven million casualties worldwide together with incalculable societal and economic consequences. The infection mechanism of SARS-Cov-2 virus begins by adhering to ACE receptors in epithelial cells of the upper respiratory tract. Uncontrolled disease can generate acute respiratory distress and multisystemic organ failure affecting the brain, heart, liver and kidney. In many COVID-19 patients, there is a need to control not only the inflammation in the lungs but also fibrosis in the kidney. Disease platforms to model and understand kidney fibrotic mechanisms after SARS-Cov-2 viral infection are lacking. The vision for such platforms is to accelerate the testing and manufacturing of therapeutic tools to mitigate kidney fibrosis in COVID-19 patients.

**Motivation and stakeholders**

iPSCs are a subset of stem cells obtained from, e.g., the skin or blood, that have been reprogrammed back to an embryonic-like state. iPSCs can be used to generate different types of cells found in the kidney. These cells can aggregate and form more complex tissue structures named organoids, which are versatile and robust enough to represent kidney’s microarchitecture and function. Kidney organoids exhibit filtration and detoxification functions, making them adequate candidates to study the nephropathology of COVID-related fibrosis. Solutions to produce a screening model to study COVID-induced kidney fibrosis should consider the needs, requirements and regulatory, financial and technical boundary conditions defined by stakeholders such as COVID-19 patients, patients with chronic kidney disease, nephrologists,

critical-care physicians, and microfabrication bioengineers.

**Problem definition**

Kidney organoids contain different functional cell types that can be found in normal kidney but their spatial organization does not reflect normal kidney architecture. Kidney fibroblasts are not normally included in kidney organoids because fibroblasts result from the differentiation of kidney organoid cells after SARS-Cov-2 stimulus. Therefore, there are no tissue engineered kidney organoids that reflect the kidney’s complex architecture and function, and that drive a specific subset of organoid cells to deposit

scar tissue to mimic fibrosis after SARS-Cov-2 infection.

**Challenge**

To generate a kidney organoid with the same anatomy and architecture as native human kidney and to guide the transition of organoid cells to fibroblasts after a viral exposure of SARS-Cov-2.

**Learning framework**

Reading the Stem Cells chapter and related literature relevant to the challenge will help you to understand:

1. The anatomy and physiology of the kidney.

2. The pathophysiology and progression of chronic kidney disease.

3. The methods and tools to generate iPSCs from somatic cells.

4. The state-of-the-art clinical strategies to mitigate kidney fibrosis.

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

5. The protocols to deliver viruses into kidney organoids.

6. The engineering strategies to fabricate organoids (integrate cells, materials, growth factors, and

biomolecules to the fabrication strategies).

7. The strategies to induce fibrosis in kidney organoids.

8. Molecular markers to validate organoid kidney models subjected to COVID-19 infection.

**End product**

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

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