# Challenge based learning (CBL)

# Engineering the next generation of functional kidney organoids

**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**

Kidney organoids can be used as kidney replacement therapy in patients with kidney failure. Even though kidney organoids derived from induced Pluripotent Stem Cells (iPSCs) can self-organize into structures that resemble fetal kidney, several limitations still exist. Namely, the highly variable differentiation of iPSCs into kidney cell types, the lack of functional vascularization within the organoid, the failed formation of collecting ducts connected to nephrons, and a functional ureter. Therefore, there is a need to reduce the demand of organ donation or the use of dialysis in patients with kidney failure via organoid technology. The long-term vision is to develop a kidney organoid that can perform diverse kidney functions including filtration of blood, secretion of endocrine and immunologic factors, reabsorption of water and electrolytes, and metabolism of minerals and nutrients.

**Motivation and stakeholders**

Chronic kidney disease affects about 13% of the global population. Due to the lack of regenerative capacity in the adult kidney, chronic kidney disease can progress to kidney failure that, in its late stages, can be treated only with dialysis or kidney transplantation. Dialysis is very costly and far from optimal because the patient is constantly bound to a machine. Additionally, there is shortage of kidneys for donation. As a result, millions of deaths occur every year because of kidney failure. Solutions to mitigate this problem should consider the needs, requirements and regulatory, financial and technical boundary conditions defined by stakeholders such as clinicians involved in precision medicine, patients, and biotech companies and research laboratories involved in organoid manufacturing.

**Problem definition**

The human kidney involves an intricate relationship of 26 different cell types to form the functional organ. Current strategies in creating kidney organoids involve the induction of iPSCs on natural or synthetic matrices with a very imprecise control over cells’ differentiation. This imprecise control results in high variability in iPSC’s phenotype and kidney organoid architecture and, therefore, it will impact greatly on organoid’s function. There is a need to improve one of the following three aspects of kidney organoid engineering, namely: a) the induction of iPSCs to form metanephric mesenchyme, b) the induction of nephron progenitor cells, and/or c) the genome editing of iPSCs for developing kidney organoids for precision medicine.

## Challenge

To propose a new engineering approach to generate a functional kidney organoid taking in consideration -one or a combination of- the needs mentioned above.

**Learning framework**

Reading the Embryogenesis chapter and relevant literature will help you to understand:

1. The role of the kidney in human physiology. List various functions performed by the kidney and its importance in maintaining homeostasis.
2. The embryologic developmental steps to generate an adult kidney. Include the cell types that make up this organ and how do they cooperate to make a functional kidney.
3. Outline the signaling pathways and associated factors responsible for kidney development and maturation. Indicate what key factors play the most important role(s).
4. Highlight the kidney functions that cannot yet be integrated in kidney organoids using iPSCs.

For a more focused examination of the challenge, read scientific literature and create a mind map to include information about the functional aspect you want to improve in this challenge:

1. The definition of an organoid and how it can be engineered/manufactured. List and explain the key components of a kidney organoid.
2. Define bottleneck(s) in developing a kidney organoid and what technical/engineering/biological limitations prevent researchers to create a kidney-like replica.
3. Highlight the state-of-the-art in engineering kidney organoids.
4. Define and understand the key approaches taken by scientists to engineer functional tissues.

**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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