# Challenge based learning (CBL)

# Perfusion of a tissue engineered islet of Langerhans

**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 survival and function of organs and tissues relies on constant irrigation and functional vascularization to provide oxygen and nutrients through arteries, and removal of toxins and metabolic by-products through veins. Neo-vascularization in embryological tissues is always on par with tissue growth: the bigger the tissue, the more vascularized it is. This biological design requirement successfully bypasses the limitation of simple diffusion of nutrients and oxygen through tissues. It is well known and documented that tissue diffusion is limited to 200 μm. The long-term vision is to obtain a fast and cost effective strategy to vascularize tissue-engineered tissues to ensure their survival and function after implantation.

**Motivation and stakeholders**

Patients suffering from type-I diabetes require daily insulin injections to control hyperglycemia after a meal. Constant glucose monitoring and insulin injections represent a burden for both patients and caretakers. Tissue engineering strategies are underway to generate functional islet of Langerhans-like organoids that can release insulin upon implantation. The islet-like organoids can be fabricated with induced pluripotent stem cells (iPSC), which are a relevant cell-source in modern tissue engineering, and should house functional vascularization for the systemic release of insulin. These organoids should sense blood glucose levels, anastomose with the host vasculature, and release insulin on demand. Solutions to include vasculature into tissue engineered islet of Langerhans should consider the needs, requirements and regulatory, financial and technical boundary conditions defined by stakeholders such as diabetes patients, internal medicine doctors, pediatricians, nutrition experts, biofabrication engineers, iPSC biologists, and biomedical engineers.

**Problem definition**

Currently, the functional cell types of a pre-vascularized islet of Langerhans organoid can be obtained by differentiation of IPSCs. However, maturation of the blood vessels and sufficient nutrient supply of the tissue requires that they are perfused during the *in vitro* culture stage. Therefore, a fully vascularized islet of Langerhans needs to be engineered to be used in patients suffering from type-I diabetes.

**Challenge**

To design a strategy to fabricate islet-of-Langerhans organoids with functional vasculature to replace continuous insulin injections in type-I diabetes patients.

**Learning framework**

Reading the Vascularization chapter and related literature will help you to understand:

1. The anatomy and physiology of islets of Langerhans.
2. The anatomy and physiology of blood vessels.
3. Physiological requirements of anastomosis.
4. Different strategies available to pre-vascularize tissues in vitro.

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

1. Current protocols to differentiate IPSCs into the functional cells of a pre-vascularized islet of Langerhans.
2. Biomaterials used to engineer pre-vascularized islets.
3. Assays used to demonstrate islet and blood vessel functionality.

**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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