

## **Challenge based learning (CBL)**

### **Novel therapies for pulmonary fibrosis due to Covid-19 infection**

**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**

In normal wound healing, the reparative fibrotic phase allows for the wound to be absorbed and the extracellular matrix to be remodeled to restore normal tissue function. In chronic inflammation, excessive generation and accumulation of collagen and other matrix proteins results in an increase in tissue stiffness and tissue dysfunction. It is well documented that about half of COVID-19 survivors will experience extensive lung fibrosis. The persistent respiratory complications may cause substantial population morbidity, long-term disability, and even death due to lung fibrosis progression. Therefore, the long-term goal of this research is to understand the process of lung fibrosis and generate an effective cell-based solution to resolve fibrosis after COVID-19 infection.

#### **Motivation and stakeholders**

Pulmonary fibrosis is a disease that occurs when the lung tissue becomes damaged and scarred. Most of these events are classified as interstitial lung diseases, because it affects the tissue around the alveolar sacs. Pulmonary fibrosis may be a secondary effect of diseases like COVID-19. Autoimmune disorders, bacterial, and viral infections (as in the case with COVID-19) may cause fibrotic changes in both the lung's upper or lower lobes and microscopic injuries to the lung. Lung damage caused by pulmonary fibrosis cannot be repaired, but medications and therapies can sometimes help ease symptoms and improve quality of life. Thus, there is a clinical need to develop tissue-engineered strategies that can halt the fibrotic signaling pathway to upregulate healing mechanisms to modulate and decrease aggressive interstitial fibrotic deposition in COVID-19 patients. Solutions to mitigate this problem should consider the needs, requirements and regulatory, financial and technical boundary conditions defined by stakeholders such as patients with COVID-19, critical-care physicians, internal medicine doctors, pneumologists, cell biologist, and tissue engineers.

#### **Problem definition**

At the moment, there are no tissue-engineered approaches to stop pulmonary fibrosis and protect patients from persistent symptoms due to "long COVID." Therefore, this challenge requires the generation of a cell experiment in which the feasibility of targeting a signaling pathway that will result in the mitigation of COVID-19-induced pulmonary fibrosis is demonstrated. The experiment can either be performed in vitro (using cultured cells), in animal models or in human patients. The motivation behind each cell and molecular strategy will have to be explained clearly, as well as the specific targets in the signaling pathway(s) to prevent interstitial lung fibrosis.

#### **Challenge**

To design and test a novel and not yet applied treatment option to resolve fibrosis in patients who developed COVID-19-induced pulmonary fibrosis.

#### **Learning framework**

Reading the Cell Signaling chapter and related literature will help you to understand the following:

1. The diseases that are associated with chronic inflammation leading to fibrosis.
2. The cell types that are associated with fibrosis in tissues and the roles they play in the disease.
3. How fibrosis leads to tissue dysfunction.
4. How fibrosis is influenced by the microenvironment of a tissue.
5. The signaling pathways that are involved in fibrosis.

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

6. Genes which are activated by fibrosis related signaling pathways.
7. Shared molecular pathways between interstitial lung disease and COVID-19 induced pulmonary fibrosis.
8. The molecular cell biology of COVID-19 induced activation of myofibroblasts in lungs.
9. Current therapies to treat COVID-induced lung fibrosis.

**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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