

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

### **Designing nerve guides for pain management**

**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**

Pain is an essential human sensation to alert us to adverse conditions, but patients suffering from chronic pain have a much reduced quality of life, and in their situation, pain does not have an important signaling function. Pain management is a very active field of research and a current concept is that the immune system and peripheral sensory nervous system communicate by molecular signaling. When the nerve is severed in the case of amputees, painful neuromas form, however nerve guides appear to reduce the risk of this occurring.

#### **Motivation and Stakeholders**

Pain sensitivity can be regulated/dysregulated by the immune system. Macrophages are able to promote and resolve pain sensitization and also T-cells play a dual role in pain sensitization. In addition to this, molecular therapeutic tools are available, such as small molecules, therapeutic antibodies, and siRNA, that can modulate the physiology of the immune system. It is therefore interesting to look into expanding on the opportunities to treat pain in amputees by using a tissue engineered implant. Future therapies should be based on molecular insight into the interplay between the immune- and nervous systems. Such therapies should be designed with the input from stakeholders such as intensive care unit doctors, nurses, physical therapists, immune engineers, and neural cell biologists.

#### **Problem definition**

Amputees suffer from painful neuromas that are regenerating nerves that are unable to find targets and bundle together.

#### **Challenge**

To develop a nerve guide that is specifically engineered to control nerve regeneration and prevent neuromas, potentially in conjunction with an external prosthetic.

#### **Learning framework**

Reading the Neural Tissue Engineering chapters and related literature will help you to understand the following:

1. Division, anatomy, and physiology of the peripheral nerve system
2. The sensory nerve system as part of the peripheral nerve system, and how the body feels pain.
3. The current state of peripheral nerve guides.
4. Conditions that exacerbate pain and how pain can evolve from acute to chronic.
5. The immune system as a pain mediator and the role of macrophages and T-cells.
6. Mechanisms of action of macrophages and T-cells to modulate pain.

For a more detailed look into your project, make a mind map summarizing the following:

7. Mechanism of action of current pain management drugs such as steroids and anti-inflammatory drugs.
8. Specific dimensions of your nerve guide, for the different animal models.
9. The molecular signals that combine to stimulate or reduce nerve regeneration.

#### **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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