PAIN-ON-CHIP

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My PhD project is "Pain on chip", an in vitro Sensitive Human Skin model for pain therapy analysis.

The main goals of this project are:

- developing an innervated human skin model

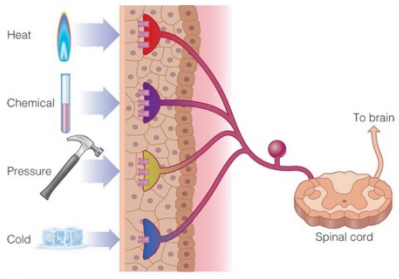
- testing the functionality of the innervated human skin model by replicating the pathological condition of pain (chemical, mechanical or thermal -induced) and recording the neurons response by electrophysiological analysis

- Understanding how to turn off the pain acting on nociceptors

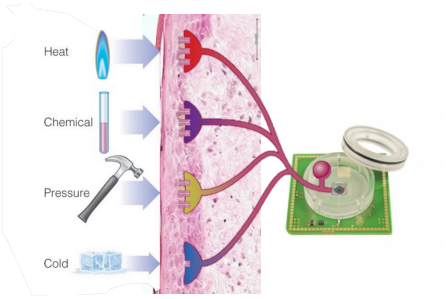
The starting point of my project is a previous work of the research group, in which a 3D innervated skin model was developed by using of mouse neurons. By means of imaging analyses they were able to demonstrate the sensory functionality of the skin by detecting, calcium ions after topical application of Capsaicin. In my project, I planned to develop a 3D innervated human skin model able to replicate the sensory function of peripheral nervous system. The strength point of the human skin model will be the dermis compartment, made up by fibroblasts embedded in their own ECM, which is the ideal context in vitro to guide the morphogenesis process of a functional neuronal network starting from neurons derived from human pluripotent stem cells. Pain will be induced by Chemical or/and mechanical agents and the signal will be recorded and decoded. The electrophysiological analysis will be performed on MEA Chip, which will be ad-hoc adapted for long-term culture of the 3D innervated skin model.

A possible field of application of the project is the development of a pain model induced by chemotherapeutic agents. In particular, some of the most used and efficient chemotherapeutic drugs induce as side effect a peripheral neuropathy also called chemically induced peripheral neuropathy (CIPN), which causes the degeneration of the neural axons, the dysfunction of the mitochondria, alterations of the sodium channels and the sensitization of the central nervous system.

IN VIVO



IN VITRO (our skin model)



There is no treatment for this type of neuropathy in the literature. So far, animal models are the most used to simulate pain, however they suffer of strongly limitation due to ethical reason and species differences. In the recent years, several 3D in vitro models have been developed to simulate the sensory ability of the skin, however these models rarely use human neuronal cells and mainly aim at rebuilding neural function and not at reproducing a pain and performing electrophysiological study.

Currently, the drugs used for pain therapy act at various levels of the Central Nervous System, resulting in a number of side effects on it. The only ones that act at the peripheral level are Local Anesthetics which inhibit sodium channels and patches based on 8% capsaicin. In fact, they have recently discovered that by using capsaicin at this concentration, it no longer has an activation effect on the TPRV1 nociceptors, but rather defunctionalises them and exerts an analgesic effect.

By coupling the 3D innervated human skin model with MEA provides a robust and reliable platform for determining the impact of a pain (such as CIPN) on the generation and propagation of the electrical signal and for developing drugs that target sensory neurons.

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