Development of a human in vitro model for pain-on-chip sensing using high-density multielectrode array (MEA) technology

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SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research

Type of method	In vitro - Ex vivo
Species from which cells/tissues/organs are derived	Human induced pluripotent stem cells
Type of cells/tissues/organs	Nociceptors (pain sensory neurons), peripheral tissue cells and CNS glial cells

DESCRIPTION

Method keywords

Nociceptors

induced pluripotent stem cells

Coculture

In vitro pain models

Analgesics

Scientific area keywords

Electrophysiology

Nociceptor

Biosensor

neuroscience

In vitro model

Method description

Chronic pain affects 20% of the population, impacting daily life and increasing psychosocial burdens for patients. Limited mechanistic understanding of human pain pathophysiology and inadequate study models, primarily rodent-based, hinder the development of effective pain medications without major side effects. In vivo, there is

extensive cellular crosstalk and pain modulation occurring between nociceptors with both peripheral tissue where pain stimuli arise and the central nervous system (CNS) where pain is perceived. Interestingly, recent momentum in in vitro models has focused on monoculture of pain sensory neurons, nociceptors. However, pain sensitization involves a cellular network communication and regulation, making single cell models limited in terms of replicating the complexities of human pain circuit. To overcome current limitations of in vitro pain modelling, we aim to mimics essential local cellular interactions of human pain circuit. Our microphysiological system (MPS) model is based on an active multielectrode array (MEA) chip, which, with its high electrode density (16,384 with a 15µm pitch) and sampling rate (30k/s), enables single-cell monitoring of nociceptors' electrical activity with high temporal resolution. The MPS-biology involves nociceptors in communication with peripheral tissue derived cells, as well as glial cells of the CNS. By applying pain stimuli and antagonists, we aim to demonstrate nociceptor firing, i.e. generating pain, and diminished firing, i.e. attenuating pain respectively. Additional aspects involve assessing differences in electrical firing when nociceptors are cultured alone versus when they include cellular interactions, gaining insights into how peripheral and central cells modulate the pain signal. This platform shows high potential to elevate our mechanistic understanding of multicellular interactions within the human pain circuit and serve as a more reliable pain-drug screening platform.

Lab equipment

(IMEC) high-density MEA chip and read-out setup Biosafety cabinet CO2 incubator Fluorescence microscope

Method status

Still in development

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

Plug-and-play Dynamic monitoring Subcellular resolution Capture cellular crosstalk of nociceptors at peripheral and central levels

Challenges

Long culture time for neuronal maturation (+20 days)

Future & Other applications

Main foreseen applications of the pain MPS are in preclinical stages of pain drugs discovery process in the biopharma industry. In the short-term, the pain MPS can be exploited at different stage of preclinical development in (1) lead identification to screen library of potential analgesic compounds and narrow down to the ones that significantly reduce the nociceptors firing, in (2) lead selection to select those that are not toxic the cells and in (3) lead optimization to study the dose effect of the potential pain medication via electrical firing monitoring. In the long term, the pain MPS could replace partially or totally animals in IND-enabling studies – requiring still for the moment mostly animal data - before going to clinical trials. Additionally, by implementing iPSC technology, there is the opportunity to develop patient-specific models to address the patient heterogeneity of pain sensing. This includes to perform ‘clinical trials-on-chip’ by stratifying patients suffering from different pain pathologies, ages or ethnicities into subgroups according to the electrophysiological readouts of their IPSC-derived pain MPS. This would allow biopharma companies to screen more targeted pain medications, ensuring the right concentration of the right drug for different types of patients. While this pain MPS is expected to be mainly of interest to biopharma companies and contract research organizations (CROs) that collaborate with them. Additionally, the cosmetics industry may also use the developed pain MPS to ensure that new products, such as skin creams, do not cause irritation or itching. The promise of this pain MPS is also to enhance our mechanistic understanding of pain. Consequently, other research institutes and university labs active in pain research, could utilize the pain MPS for mechanistic studies.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

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Associated documents

Khosrowshahi et al. - 2025 - Decoding Pain Next-Generation In Vitro Systems for Mechanistic Insights and Drug Discovery.pdf

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