Developing human cellular phenotypic assays for pain
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2. Approach & Methodology

- Human cellular models of disease developed using induced pluripotent stem cells (iPSCs) has facilitated wide-ranging research from investigation of human disease mechanisms to phenotypic drug screens.

- Pain sensation is mediated by two major subsets of primary nociceptor neurons – peptidergic and non-peptidergic that contribute to different types of noxious sensation.

- Peptidergic sensory neurons play a crucial role in inflammatory and neuropathic pain, and release the neuropeptide CGRP that plays a prominent role in the pathophysiology of pain.

- Patient iPSC-based cellular phenotypic assays, such as nociceptor hyper-excitability and CGRP release have great potential in investigating pain mechanisms and to identify novel drug targets for pain disorders.

1. Challenge

The development of new effective pain treatments is hampered by lack of relevant and reliable experimental human models.

3. Results: Directed differentiation of peptidergic sensory neurons

- Overview of TG nociceptor differentiation
- Cultures enables CGRP release and generates a homogenous and functional peptidergic population
- Reproducible peptidergic differentiation across multiple lines

Multielectrode array (MEA) based high throughput screening platform

- MEA – set up
- Validation of MEA 'hits' – Firing frequency
- Validation of MEA 'hits' – Number of burst
- Validation of MEA 'hits' – Spikes per burst

Impact & take home message
Human cellular models of pain will enable identification of new effective therapies

Value of IMI collaboration
Knowledge exchange and shared purpose to achieve translational neuroscience and patient benefit

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