10 YEARS OF BREAKTHROUGHS
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stem BANCC
Stem Cells for Drug Discovery

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Developing human cellular phenotypic assays for pain

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Facts & Figures

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Contributions	
IMI funding:	26 000 000 €
EFPIA in kind:	20 761 386 €
Other:	8 249 094 €
Total Cost:	55 010 480 €

Project website: www.stembancc.org

Social media: @CaderLab

1. Challenge

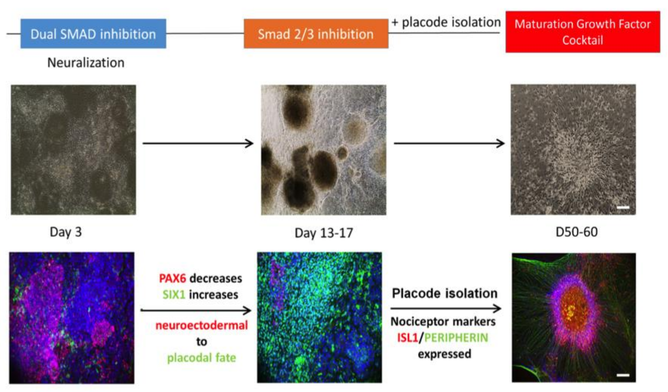
The development of new effective pain treatments is hampered by lack of relevant and reliable experimental human models.

2. Approach & Methodology

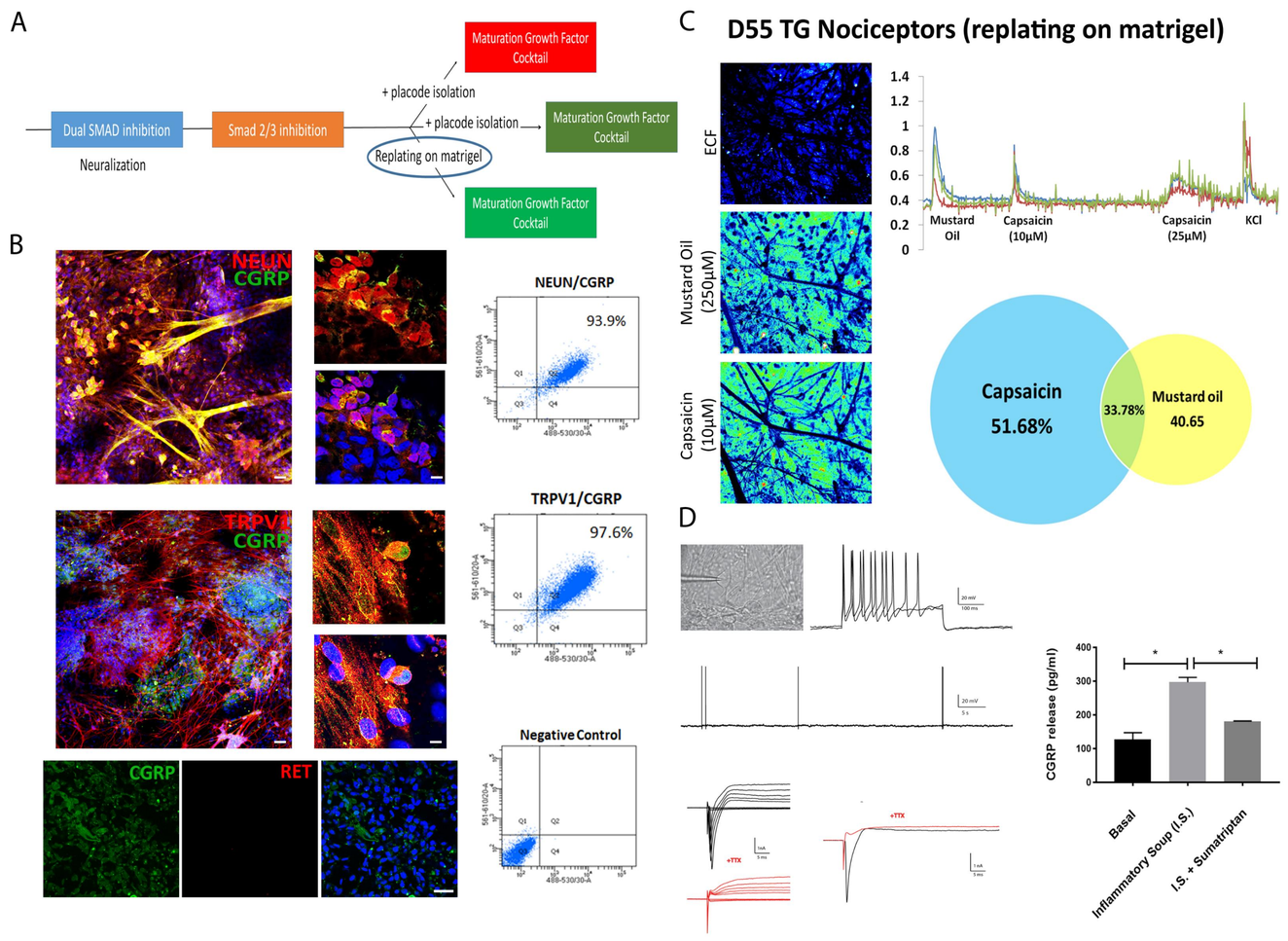
- Human cellular models of disease developed using induced pluripotent stem cells (iPSCs) has facilitated wide-ranging research from investigation of human disease mechanisms to phenotypic drug screens.
- Pain sensation is mediated by two major subsets of primary nociceptor neurons – peptidergic and 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.

3. Results: Directed differentiation of peptidergic sensory neurons

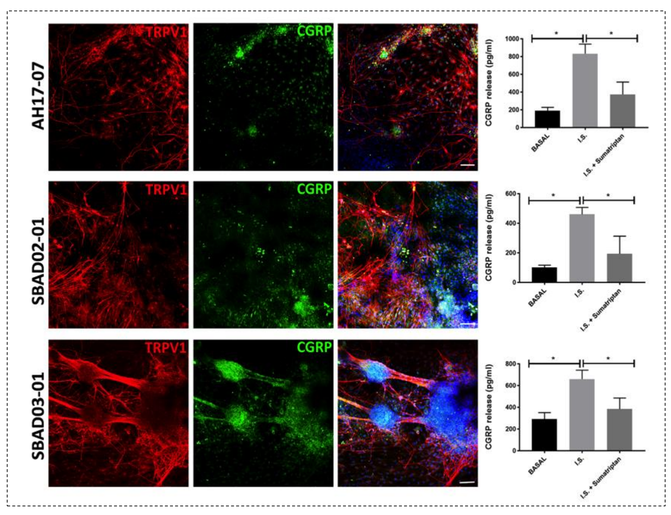
A Overview of TG nociceptor differentiation



B Cultures enables CGRP release and generates a homogenous and functional peptidergic population

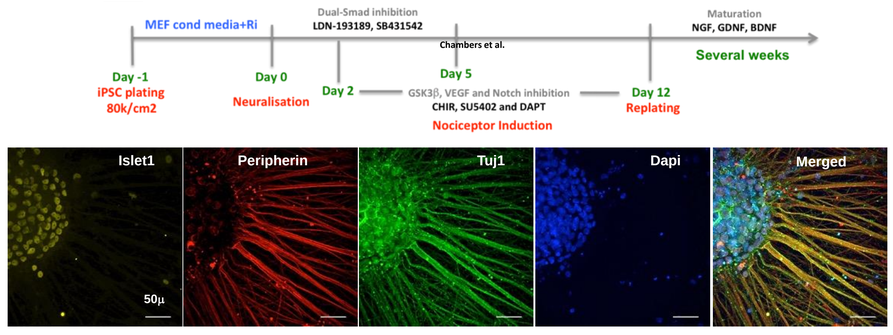


C Reproducible peptidergic differentiation across multiple lines

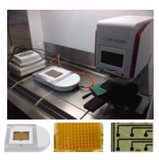


Multielectrode array (MEA) based high throughput screening platform

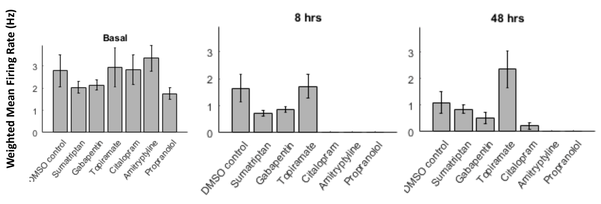
A Differentiation of dorsal root ganglia nociceptors



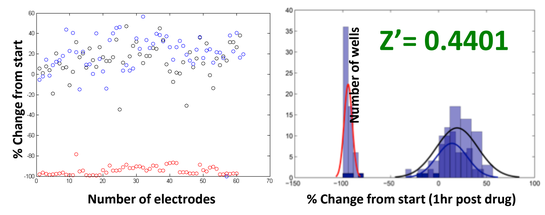
B MEA – set up



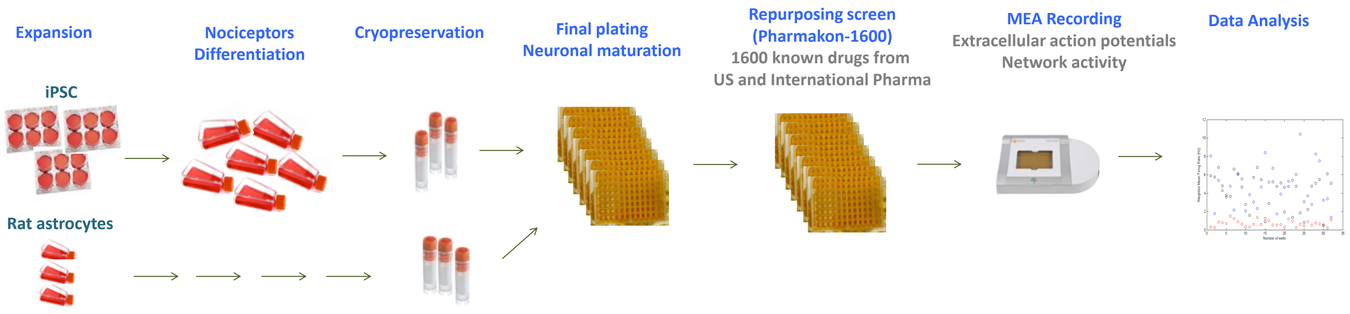
C Screening commonly used migraine drugs



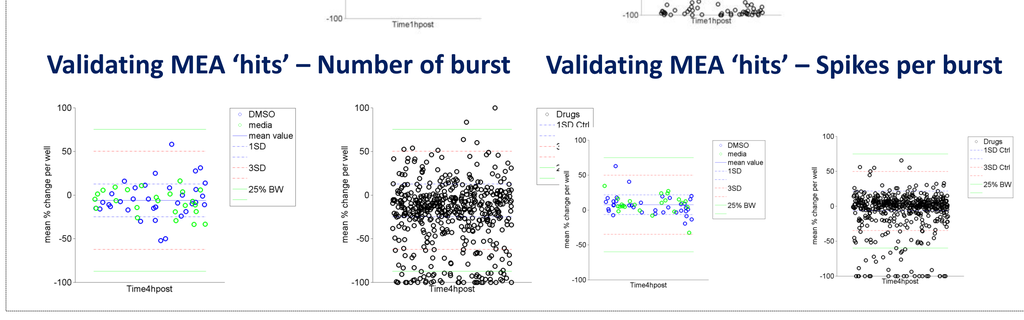
D Z-factor



E MEA-HTS Workflow



F Validating MEA 'hits' – Firing frequency



Validating MEA 'hits' – Number of burst

Validating 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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