An in vitro model of nociceptors in human trigeminal nerves

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Background: The oro-facial region is densely innervated by the trigeminal nerve, which when stimulated can induce noxious pain sensation and contribute to neurogenic inflammation in local tissues. Recent research on the expression of specialised ion channels on the trigeminal nerve has highlighted the need to undertake more extensive studies on ion channel expression/functionality with the aim of elucidating their role in pain sensations. A major family of such ion channels is the transient receptor potential (TRP) channels which are activated by a wide variety of thermal, mechanical or chemical stimuli and merit investigation as possible druggable targets for future analgesics.

Objectives: Study of TRP channel expression and regulation in oro-facial tissues is hindered by the fact that the cell bodies of neurons innervating these tissues are located in the trigeminal ganglion. Using dental pulp stem cells differentiated towards peripheral neuronal equivalents (PNEs) we sought to study TRP channels on human neuronal cells and determine whether their expression is regulated by inflammatory cytokines.

Methods: Dental pulp stem cells (DPSCs) were grown on substrate-coated tissue culture plates and differentiated towards a neuronal phenotype using neuronal induction media. RNA was extracted from PNEs +/- cytokine treatment. The RNA was then reverse transcribed into cDNA and quantified by the quantitative polymerase chain reaction (qPCR).

Results: qPCR analysis showed that PNEs expressed the TRP channels TRPA1, TRPV1, TRPV4 and TRPM8. TRPA1 was the most abundantly expressed TRP channel of those studied whereas TRPM8 was lowly expressed. TRP channel expression was shown to be regulated by treatment with inflammatory cytokines.

Conclusion: PNEs differentiated from DPSCs provide a suitable model for TRP channel expression and regulation in oro-facial tissues. This human neuronal model has potential for use in pre-clinical studies of novel analgesics.

Keywords: Pain, inflammation, TRP channels, trigeminal

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