**Characterising Phytocannabinoids at the Cellular Ageing and Pain Target –TRPA1**

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**Background and aims.** TRPA1 is a non-selective cation channel that is activated by a broad range of stimuli including temperature changes, mechanical stimulus, reactive products (e.g. electrophiles & reactive oxygen species), and both endogenous and exogenous cannabinoids. The majority of research on this channel has focused on its involvement in nociceptive and inflammatory signalling, with the aim of developing antagonists as therapeutics to limited success. This may be because TRPA1 has more recently been implicated in neuroprotective and pro-longevity pathways.1,2,3

Different ligands, like cannabinoids, have been found to activate TRPA1 in distinct ways, with some altering the pathways signalled (e.g. activation without pain), leading to the potential of using cannabinoids as lead TRPA1 agonists in developing novel therapeutics that bias the neuroprotective and pro-longevity pathways. Previous studies have only characterised cannabinoids at the rat homologue of TRPA1, for which some ligands can have differential pharmacological activity to the human channel.4,5 **Aim:** We sought to characterise these cannabinoids at the human TRPA1receptor in vitro, with the addition of nine previously uncharacterised minor phytocannabinoids.

**Methods.** Cannabinoids were characterised using the FLIPR calcium imaging dye Calcium 5 and measured with the Flexstation 3 plate reader in 96-well format. Human TRPA1 was stably transfected in HEK293 Flip-In T-REx cells, with the channel’s expression being induced the day before experiments.

**Results.** The 11 characterised cannabinoids had a different potency to previous studies using the rat form of the channel. The addition of 9 minor phytocannabinoids being characterised at TRPA1. A few cannabinoids stood out as having a higher or similar potency than our positive control cinnamaldehyde (CIN): CBCV>CBNA>CBDV>CBC**>CIN>**THC>CBD>CBCA.

**Conclusion/Discussion.** TRPA1 activation in both *C. elegans* and human cells has been shown to signal and induce cellular changes that are pro-adaptive against certain forms of reactive products (i.e. ROS, glyoxals, and protein aggregates) encountered and produced during the cellular ageing process.1,2,3  Phytocannabinoids form the starting point in finding and developing a selective cannabinoid-like agonist of TRPA1, with the aim of using cannabinoid-like drugs to induce cellular adaptive changes to ameliorate certain conditions encountered in age related decline (i.e. diabetic neuropathy) and induce pro-longevity in *C. elegans* models of ageing and age-related diseases.

**References:**

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