

2.3

Responses of the Salivary Proteome to Transient Receptor Potential Channel Agonists

Jack Houghton (King's College London), **Joachim Hans** (Symrise AG), **Manuel Pesaro** (Symrise AG), **Jakob Ley** (Symrise AG), **Guy Carpenter** (King's College London), **Gordon Proctor** (King's College London)

Transient Receptor Potential (TRP) channel agonists have been shown to increase salivary flow rate and modify the physical properties of saliva but there are no studies investigating their effects on the salivary proteome. The aim of this study was to investigate how the whole mouth saliva (WMS) proteome is affected by the TRP channel agonists; nonivamide (TRPV1 agonist, capsaicin analogue), menthol (TRPM8 agonist) and cinnamaldehyde (TRPA1 agonist).

WMS was collected after mouth-rinsing with water, nonivamide, cinnamaldehyde and propylene glycol (vehicle) at concentrations just above their detection thresholds (determined by the 3-AFC method). The proteomes of collected WMS were analysed by relative-quantitative LC-MS/MS. In a follow up study, nonivamide, cinnamaldehyde, propylene glycol and menthol were used at concentrations previously determined to be strong sensory stimuli. WMS was collected before and for two minutes after mouth-rinsing with water and each compound. The proteomes of collected WMS were analysed by TMT-labelled absolute-quantitative LC-MS/MS. Following mild stimulation, 36 of 1026 identified proteins showed a significant fold-change from the post-water sample. Clustering analysis determined that variation was participant rather than stimulus dependent.

Following stronger stimulation, 522 proteins were identified and clustering determined that proteome changes were more mouth-rinse dependent. Protein fold-changes reflected altered biological process and function of the proteome in a gene ontology analysis. Nonivamide and menthol mouth-rinses increased submandibular gland associated proteins whilst cinnamaldehyde increased parotid gland associated proteins.

We demonstrate that the WMS proteome varies in its response to TRP channel agonists. When the stimuli are at the detection threshold, most of the variation is seen between individuals but more strongly stimulating concentrations cause compound specific changes. These compositional changes reflect biological process and function as well as differences in how the major glands contribute to the stimulated WMS proteome giving insight into the mechanism responsible for the differing responses.