Synopsis of Original Research Paper

Functional expression of the bitter taste receptors in human keratinocytes

Motonao Nakamura

Department of Life Science, Faculty of Science, Okayama University of Science

G-protein coupled receptors (GPCRs) are pivotal targets in medical and pharmaceutical research fields because a wide variety of disease-related processes are critically controlled by the signal transduction mediated by these receptors. Type 2 better taste receptors (TAS2Rs) comprise a large family of GPCRs with 25 distinct isoforms encoded in the human genome. Recent studies have shown that TAS2Rs are not only expressed in the taste buds of the tongue, but also in the skin. In the present study, we showed the functional expression of all human TAS2Rs in the human keratinocytes. Interestingly, these TAS2R proteins are not localized on the plasma membrane, mainly detected in the cytoplasmic regions in the immune-fluorescent staining experiments of the keratinocytes. The expressions of TAS2Rs in these cells were enhanced by the stimulation with bitter compounds, such as denatonium, diphenhydramine and saccharine. Furthermore, the stimulation of bitter compounds further increased the expression of three ABC-transporters, ABC-B1, ABC-C1 and ABC-G2, which are involving in the multidrug-resistance of various cancer cells. These results raise the possibility that the activation of TAS2Rs by the bitter compounds enhances the exclusion of these substances from the keratinocytes through the ABC-transporters. The analyses of the signaling pathway evoked by the TAS2Rs revealed the coupling of these receptors with Gαi and/or Gα12/13, followed by the activation of NF-κB. Together, these results suggest that the keratinocytes possess TAS2Rs in the cytoplasmic organelles, and recognize the infiltrated substances, including bitter compounds, resulting in the activation of the ABC-transporters, such as ABC-B1, ABC-C1 and ABC-G2, to exclude the substances.