האוניברסיטה העברית בירושלים
הפקולטה לחקלאות, מזון וסביבה ע"ש רוברט ה. סמית
המכון לביוכימיה, מדעי המזון והתזונה

הרצאת התקדמות לתואר שלישי

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הנושא:

The effect of amphipathic tastants on the desensitization pathway of the sweet taste receptors

המפגש יתקיים
ביום חמישי, 19 מרץ 2015, בשעה 12:00
בחדר 3114 בבניין מדעי הצמח

Abstract:

Bitter and sweet tastants stimulate taste sensation via specific G-protein-coupled receptors (GPCRs) present on the plasma membrane of certain taste cells. T2Rs are bitter taste GPCRs and T1R2/T1R3 are sweet taste GPCRs. In contrast to sugars, most bitter tastants and non-sugar sweeteners are amphipathic molecules that are known to produce a delay in taste onset and in taste termination termed "lingering aftertaste". The molecular basis for this phenomenon is not known. The present hypothesis suggests that amphipathic tastants, in addition to their binding to taste GPCRs, permeate the cells and inhibit the phosphorylation of certain signal-termiation kinases such as PKA and GRKs, and thus inhibit desensitization. Because the desensitization of the T1R/T2R taste receptors has not yet been studied, β2-adrenergic receptor (β2AR) was first used as a well-established model for GPCR desensitization. Experiments using cells expressing the β2AR indicated that amphipathic tastants, due to their permeation into the cytosol, inhibit GRK2, and consequently amplify β2AR signaling to delay of β2AR desensitization. Next, I explored whether the same phenomenon is observed in cells expressing the T1R2/T1R3. Following stimulation of HEK293T expressing T1R2/T1R3 by different sweeteners, IP1 (a convenient readout for IP3) responses were monitored to represent the activity of PLCβ2, an essential pathway for the sensation of sweet taste in mammals. Both dose response and time course were worked out. Most important, similar to the results observed with the β2AR model, preincubation of HEK293T cells expressing T1R2/T1R3 but not bitter taste receptors with membrane permeable bitter tastants, amplified significantly the IP1 responses due to stimulation by various sweeteners. Although the results are similar to those obtained by the β2AR model, the exact role of GPCR kinases remained to be elucidated.
In conclusion, these results provide evidence that amphipathic tastants can, after reaching the cell cytosol, affect GRK2 activity, thereby inhibiting the progression of the □2AR-desensitization pathway. In addition, the amphipathic tastants, due to their permeation, also amplify the activity of the sweet receptor. Since these tastants are components of our daily diets and should have access to other tissues, they may affect different physiological events that are not related to taste.

סגל וסטודנטים מוזמנים להשתתף