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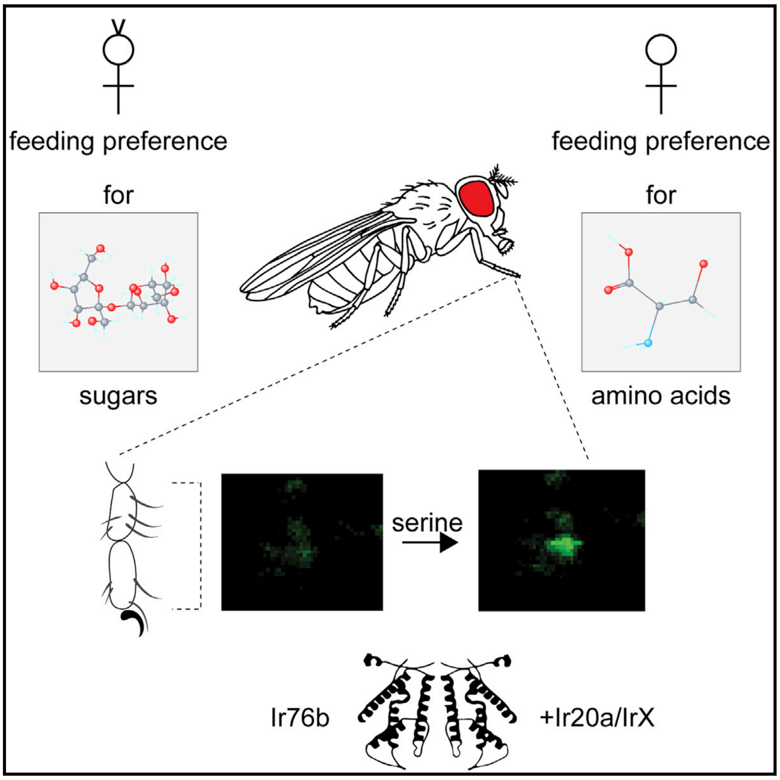
Article

A Molecular and Cellular Context-Dependent Role for Ir76b in Detection of Amino Acid Taste

Graphical Abstract



Authors

Anindya Ganguly, Lisa Pang, Vi-Khoi Duong, Angelina Lee, Hanni Schoniger, Erika Varady, Anupama Dahanukar

Correspondence

anupama.dahanukar@ucr.edu

In Brief

Ganguly et al. demonstrate that Ir76b mediates cellular and behavioral responses to amino acids that underlie post-mating yeast and amino acid feeding preferences of *Drosophila* females. Ir20a, possibly one among many factors, plays a role in changing Ir76b activity from an ungated salt receptor to an amino-acid-gated receptor.

Highlights

- *Drosophila* females display amino acid feeding preference after mating
- Taste neurons in female tarsi are activated by amino acids
- A highly conserved receptor, Ir76b, is required for amino acid taste
- Ir20a mediates amino acid taste and blocks salt taste dependent on Ir76b

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A Molecular and Cellular Context-Dependent Role for Ir76b in Detection of Amino Acid Taste

Anindya Ganguly,[1] Lisa Pang,[2] Vi-Khoi Duong,[3] Angelina Lee,[4] Hanni Schoniger,[3] Erika Varady,[3] and Anupama Dahanukar[1,2,5,*]
[1]Interdepartmental Neuroscience Program
[2]Department of Entomology
[3]University Honors Program
[4]Undergraduate Anthropology Major
University of California, Riverside, CA 92521, USA
[5]Lead Contact
*Correspondence: anupama.dahanukar@ucr.edu
http://dx.doi.org/10.1016/j.celrep.2016.12.071

SUMMARY

Amino acid taste is expected to be a universal property among animals. Although sweet, bitter, salt, and water tastes have been well characterized in insects, the mechanisms underlying amino acid taste remain elusive. From a *Drosophila RNAi* screen, we identify an ionotropic receptor, Ir76b, as necessary for yeast preference. Using calcium imaging, we identify *Ir76b*$^+$ amino acid taste neurons in legs, overlapping partially with sweet neurons but not those that sense other tastants. *Ir76b* mutants have reduced responses to amino acids, which are rescued by transgenic expression of *Ir76b* and a mosquito ortholog *AgIr76b*. Co-expression of Ir20a with Ir76b is sufficient for conferring amino acid responses in sweet-taste neurons. Notably, Ir20a also serves to block salt response of Ir76b. Our study establishes the role of a highly conserved receptor in amino acid taste and suggests a mechanism for mutually exclusive roles of Ir76b in salt- and amino-acid-sensing neurons.

INTRODUCTION

The importance of dietary protein and amino acids has been investigated for several insects including *Drosophila* and reveals that, like mammals, insects must acquire some essential amino acids via foods (Golberg and De Meillon, 1948; Hinton et al., 1951; House, 1962; Singh and Brown, 1957). Females, in particular, require large supplies of amino acids for synthesizing egg yolk (Dimond et al., 1956). Restriction of amino acids thus has a direct impact on female fecundity (Chang, 2004; Dimond et al., 1956; Fink et al., 2011). Amino acid deprivation also significantly affects larval growth and development, as well as adult lifespan (Baltzer et al., 2009; Britton and Edgar, 1998; Chang, 2004; Grandison et al., 2009; Vrzal et al., 2010).

Given the importance of amino acids in food sources, it is perhaps not surprising that insects demonstrate taste sensitivity to amino acids. Behavioral analyses in various insects, including honeybees, ants, and the dengue fever vector, *Aedes aegypti*, show that mixtures of some amino acids and sugar are preferred over sugar alone (Alm et al., 1990; Ignell et al., 2010; Wada et al., 2001). Moreover, electrophysiological recordings show that selected amino acids evoke action potentials in taste hairs of some insects. For instance, in blowflies and fleshflies some individual amino acids were found to activate either sweet- or salt-sensing neurons; others were found to have inhibitory effects on these taste neurons (Shiraishi and Kuwabara, 1970). Studies in blood-feeding tsetse flies identified neurons in tarsal taste hairs that are exquisitely sensitive to several individual amino acids, as well as to a mixture of amino acids found in human sweat (Van der Goes van Naters and den Otter, 1998). Amino-acid-sensing neurons have also been described in cabbage butterflies (Van Loon and Van Eeuwijk, 1989) and *Helicoverpa* moths (Zhang et al., 2011; Zhang et al., 2010).

Drosophila exhibit strong feeding preference for yeasts and yeast extract, which serve as a major source of protein (Tatum, 1939). Mated females, as well as adult flies fed on a protein deficient diet, can identify and select yeast over sucrose in binary choice assays (Ribeiro and Dickson, 2010; Vargas et al., 2010). A recent study reports behavioral taste sensitivity to free amino acids, albeit only in flies raised on a diet lacking in protein (Toshima and Tanimura, 2012). In these experiments, flies extended their proboscis upon stimulation of taste hairs with amino acid solutions, indicating a role for taste hairs as amino acid sensors. However, little is known about the molecular and cellular basis of amino acid taste.

Many amino acids taste savory or sweet to humans. Mammals detect amino acids using a heteromeric receptor comprised of two subunits, T1R1 and T1R3, expressed in fungiform taste buds (Nelson et al., 2002). The T1R1/T1R3 receptor has broad specificity for L-amino acids and does not respond to the D isomers. T1Rs, which are G-protein-coupled receptors related to metabotropic glutamate receptors, have no counterparts in insect genomes.

Here, we investigated behavioral and cellular responses in the fly to amino acids, identifying them as critical cues for feeding preference to yeast extract. We find that mated females exhibit feeding preference for individual amino acids, which are