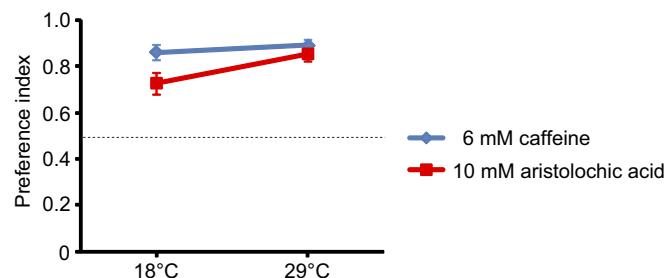


# Supporting Information

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**Fig. S1.** Taste preferences for aristolochic acid and caffeine at 18 °C and 29 °C. Wild-type flies were allowed to select 1 mM sucrose alone vs. 5 mM sucrose with either 6 mM caffeine or 10 mM aristolochic acid. Binary food-choice assays were performed at 18 °C or 29 °C. P.I.'s for 6 mM caffeine: 18 °C, 0.86 ± 0.03; 29 °C, 0.89 ± 0.03. *P* value = 0.52. P.I.s for 10 mM aristolochic acid: 18 °C, 0.73 ± 0.05; 29 °C, 0.85 ± 0.03. *P* value = 0.10. *n* = 3 for all experiments.

**Table S1. Statistics for the data shown in Fig. 2A**

| Compounds         | Wild type                | <i>trpA1</i> <sup>†</sup> |
|-------------------|--------------------------|---------------------------|
| Sucrose           |                          |                           |
| P.I.              | 0.05 ± 0.00*             | 0.03 ± 0.01               |
| <i>P</i> values   |                          | 0.23                      |
| Caffeine          |                          |                           |
| P.I.              | 0.95 ± 0.01              | 0.94 ± 0.01               |
| <i>P</i> values   |                          | 0.79                      |
| Quinine           |                          |                           |
| P.I.              | 0.93 ± 0.02              | 0.97 ± 0.01               |
| <i>P</i> values   |                          | 0.075                     |
| Denatonium        |                          |                           |
| P.I.              | 0.96 ± 0.01              | 0.96 ± 0.01               |
| <i>P</i> values   |                          | 0.86                      |
| Berberine         |                          |                           |
| P.I.              | 0.91 ± 0.01              | 0.93 ± 0.01               |
| <i>P</i> values   |                          | 0.24                      |
| Lobeline          |                          |                           |
| P.I.              | 0.95 ± 0.01              | 0.95 ± 0.01               |
| <i>P</i> values   |                          | 0.73                      |
| Papaverine        |                          |                           |
| P.I.              | 0.92 ± 0.00 <sup>‡</sup> | 0.94 ± 0.01               |
| <i>P</i> values   |                          | 0.10                      |
| Strychnine        |                          |                           |
| P.I.              | 0.95 ± 0.01              | 0.97 ± 0.00 <sup>‡</sup>  |
| <i>P</i> values   |                          | 0.24                      |
| Aristolochic acid |                          |                           |
| P.I.              | 0.80 ± 0.02              | 0.35 ± 0.02               |
| <i>P</i> values   |                          | 4.6 × 10 <sup>-8</sup>    |

The preference indexes (P.I.s) are listed. *n* ≥ 4 (40–60 flies per experiment) for the behavioral assays. The *P* values are based on the unpaired Student's *t* test and are relative to wild type unless specified.

\*0.004.

<sup>†</sup>0.003.

<sup>‡</sup>0.005.

**Table S2.** Statistics for the data shown in Fig. 2B

| Genotype                             | P.I.        | P values               |
|--------------------------------------|-------------|------------------------|
| Wild type                            | 0.80 ± 0.02 |                        |
| <i>trpA1</i> <sup>1</sup>            | 0.35 ± 0.02 | 4.6 × 10 <sup>-8</sup> |
| <i>pyx</i> <sup>ex</sup>             | 0.74 ± 0.04 | 0.18                   |
| <i>wtrw</i> <sup>ex</sup>            | 0.80 ± 0.01 | 0.99                   |
| <i>pain</i> <sup>1</sup>             | 0.74 ± 0.03 | 0.15                   |
| <i>trp</i> <sup>P343</sup>           | 0.77 ± 0.04 | 0.53                   |
| <i>trp</i> <sup>B02</sup>            | 0.71 ± 0.04 | 0.071                  |
| <i>trp</i> <sup>γ</sup> <sup>1</sup> | 0.73 ± 0.02 | 0.094                  |
| <i>iav</i> <sup>1</sup>              | 0.77 ± 0.04 | 0.50                   |
| <i>nan</i> <sup>36a</sup>            | 0.79 ± 0.05 | 0.79                   |

The preference indexes (P.I.s) are listed.  $n \geq 4$  (40–60 flies per experiment) for the behavioral assays. The P values are based on the unpaired Student's t test and are relative to wild type unless specified.

**Table S3.** Statistics for the data shown in Fig. 2C

| Genotype | Wild type   | <i>trpA1</i> <sup>1</sup> | <i>trpA1</i> <sup>GAL4</sup> | <i>trpA1</i> <sup>ins</sup> |
|----------|-------------|---------------------------|------------------------------|-----------------------------|
| P.I.     | 0.80 ± 0.02 | 0.35 ± 0.02               | 0.31 ± 0.03                  | 0.34 ± 0.05                 |
| P values |             | 4.6 × 10 <sup>-8</sup>    | 1.86 × 10 <sup>-7</sup>      | 2.5 × 10 <sup>-4</sup>      |

The preference indexes (P.I.s) are listed.  $n \geq 4$  (40–60 flies per experiment) for the behavioral assays. The P values are based on the unpaired Student's t test and are relative to wild type unless specified.

**Table S4.** Statistics for the data shown in Fig. 2D

| Genotype                               | P.I.        | P values               | P values*              | P values†              |
|--|-------------|------------------------|------------------------|------------------------|
| Wild type                              | 0.80 ± 0.02 |                        |                        |                        |
| <i>UAS-trpA1;trpA1</i> <sup>1</sup>    | 0.36 ± 0.02 | 3.5 × 10 <sup>-7</sup> | 6.0 × 10 <sup>-9</sup> | 3.4 × 10 <sup>-5</sup> |
| <i>trpA1</i> <sup>GAL4</sup>           | 0.31 ± 0.03 | 1.9 × 10 <sup>-7</sup> | 2.5 × 10 <sup>-5</sup> |                        |
| <i>UAS-trpA1;trpA1</i> <sup>GAL4</sup> | 0.72 ± 0.02 | 0.056                  |                        |                        |
| <i>Gr66a-Gal4;trpA1</i> <sup>1</sup>   | 0.32 ± 0.03 | 7.0 × 10 <sup>-6</sup> |                        | 3.6 × 10 <sup>-5</sup> |
| <i>Gr66a-Gal4, UAS-trpA1;trpA1</i>     | 0.67 ± 0.03 | 0.010                  |                        |                        |

The preference indexes (P.I.s) are listed.  $n \geq 4$  (40–60 flies per experiment) for the behavioral assays. The P values are based on the unpaired Student's t test and are relative to wild type unless specified.

\*Relative to *UAS-trpA1;trpA1*<sup>GAL4</sup>.

†Relative to *Gr66a-Gal4, UAS-trpA1;trpA1*.

**Table S5.** Statistics for the data shown in Fig. 3A

| Compounds         | Wild type    | <i>trpA1</i> <sup>1</sup> |
|-------------------|--------------|---------------------------|
| Sucrose           |              |                           |
| Spikes/0.5 sec    | 18.71 ± 2.06 | 15.14 ± 1.74              |
| P values          |              | 0.21                      |
| Caffeine          |              |                           |
| Spikes/0.5 sec    | 10.29 ± 1.09 | 9.57 ± 2.56               |
| P values          |              | 0.79                      |
| Quinine           |              |                           |
| Spikes/0.5 sec    | 7.43 ± 1.69  | 10.71 ± 1.06              |
| P values          |              | 0.13                      |
| Denatonium        |              |                           |
| Spikes/0.5 sec    | 11.86 ± 1.64 | 11.14 ± 3.54              |
| P values          |              | 0.86                      |
| Berberine         |              |                           |
| Spikes/0.5 sec    | 13.86 ± 2.24 | 12.13 ± 1.61              |
| P values          |              | 0.53                      |
| Lobeline          |              |                           |
| Spikes/0.5 sec    | 11.00 ± 1.40 | 12.22 ± 0.97              |
| P values          |              | 0.48                      |
| Papaverine        |              |                           |
| Spikes/0.5 sec    | 11.25 ± 1.30 | 8.33 ± 1.35               |
| P values          |              | 0.14                      |
| Strychnine        |              |                           |
| Spikes/0.5 sec    | 5.75 ± 1.24  | 4.00 ± 1.31               |
| P values          |              | 0.35                      |
| Aristolochic acid |              |                           |
| Spikes/0.5 sec    | 7.69 ± 1.79  | 0.22 ± 0.22               |
| P values          |              | 0.51 × 10 <sup>-2</sup>   |

The spike frequencies (±SEMs) are listed.  $n \geq 7$  for the tip recordings. The P values are based on the unpaired Student's *t* test and are relative to wild type unless specified.

**Table S6.** Statistics for the data shown in Fig. 3C

| Genotype                                       | Spikes/0.5 sec | P values               | P values*              |
|--|----------------|------------------------|------------------------|
| Wild type                                      | 7.69 ± 1.79    |                        |                        |
| <i>trpA1</i> <sup>1</sup>                      | 0.22 ± 0.22    | 5.1 × 10 <sup>-3</sup> |                        |
| <i>trpA1</i> <sup>ins</sup>                    | 1.25 ± 0.67    | 2.1 × 10 <sup>-2</sup> |                        |
| <i>trpA1</i> <sup>GAL4</sup>                   | 0.67 ± 0.67    | 8.9 × 10 <sup>-3</sup> |                        |
| <i>UAS-trpA1;trpA1</i> <sup>GAL4</sup>         | 10.86 ± 3.68   | 0.39                   | 5.3 × 10 <sup>-3</sup> |
| <i>Gr66a-GAL4,UAS-trpA1;trpA1</i> <sup>1</sup> | 6.20 ± 0.85    | 0.47                   | 2.2 × 10 <sup>-5</sup> |

The spike frequencies (±SEMs) are listed.  $n \geq 7$  for the tip recordings. The P values are based on the unpaired Student's *t* test and are relative to wild type unless specified.

\*Relative to *trpA1*<sup>1</sup>.

**Table S7. Statistics for the data shown in Fig. 5A**

| Genotype   | P.I.        | <i>P</i> values        | <i>P</i> values* |
|--|-------------|------------------------|------------------|
| Wild type  | 0.80 ± 0.02 |                        |                  |
| <i>norpA</i> <sup>P24</sup>  | 0.54 ± 0.06 | 9.8 × 10 <sup>-3</sup> |                  |
| <i>norpA</i> <sup>P54</sup>  | 0.59 ± 0.03 | 1.0 × 10 <sup>-3</sup> |                  |
| <i>norpA</i> <sup>P24</sup> ;UAS- <i>norpA</i> ;trpA1 <sup>GAL4</sup> /+ | 0.81 ± 0.01 | 0.79                   | 0.010            |

The preference indexes (P.I.s) are listed.  $n \geq 4$  (40–60 flies per experiment) for the behavioral assays. The *P* values are based on the unpaired Student's *t* test and are relative to wild type unless specified.

\*Relative to *norpA*<sup>P24</sup>.

**Table S8. Statistics for the data shown in Fig. 5B**

| Genotype   | Spikes/0.5 sec | <i>P</i> values        | <i>P</i> values*       |
|--|----------------|------------------------|------------------------|
| Wild type  | 7.69 ± 1.79    |                        |                        |
| <i>norpA</i> <sup>P24</sup>  | 2.41 ± 0.60    | 3.3 × 10 <sup>-3</sup> |                        |
| <i>norpA</i> <sup>P54</sup>  | 1.15 ± 0.62    | 3.9 × 10 <sup>-3</sup> |                        |
| <i>norpA</i> <sup>P24</sup> ;UAS- <i>norpA</i> ;trpA1 <sup>GAL4</sup> /+ | 11.89 ± 3.43   | 0.24                   | 3.4 × 10 <sup>-4</sup> |

The spike frequencies ( $\pm$ SEM) are listed.  $n \geq 7$  for the tip recordings. The *P* values are based on the unpaired Student's *t* test and are relative to wild type unless specified.

\*Relative to *norpA*<sup>P24</sup>.