# RNA editing plays critical role in fruit flies' sense of smell and social interactions

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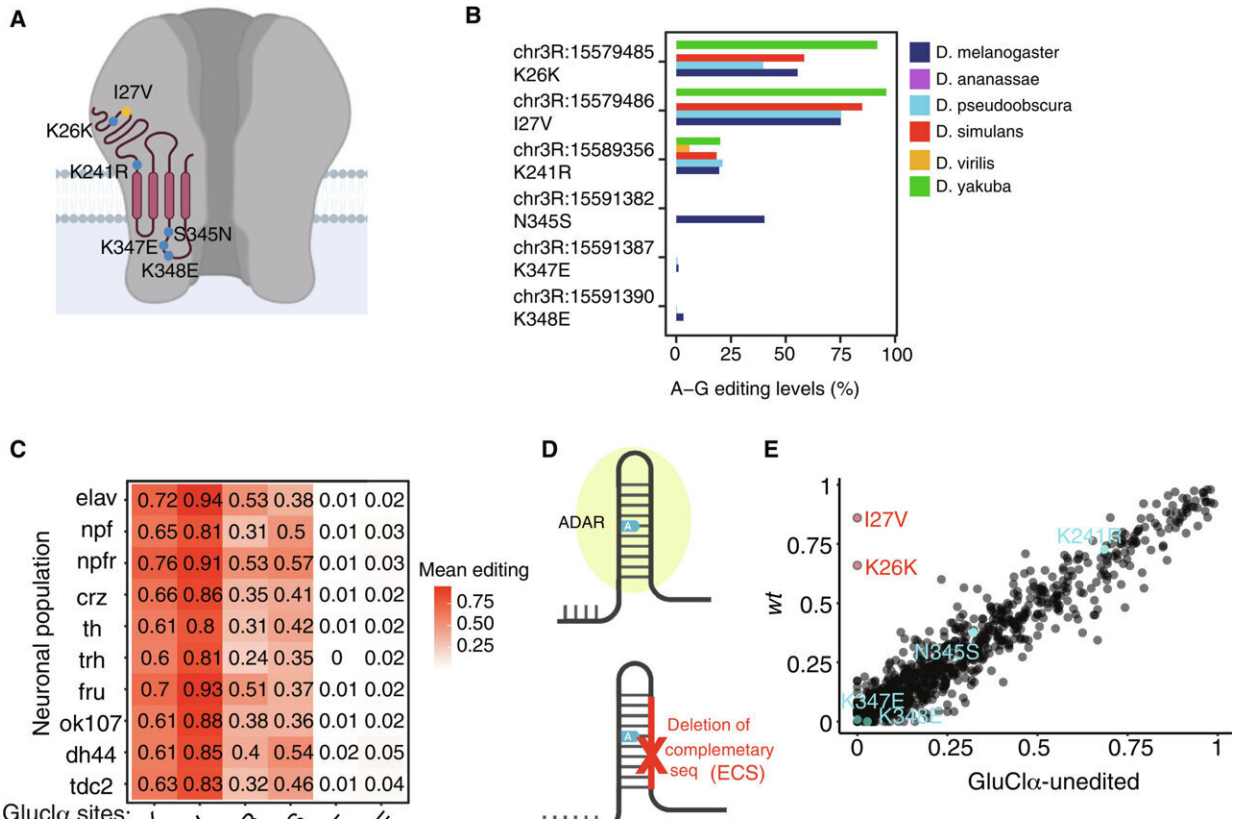


The recoding of Ile$^{27}$ to Val is conserved across Drosophila species. Credit: *Science Advances* (2024). DOI: 10.1126/sciadv.adi9101

Imagine your DNA as a set of instructions or a recipe book that tells your body how to make everything it needs to function, from proteins to

cells. Every time the body needs to build something, it reads these instructions. But sometimes, the body can make small edits to these instructions—this is where RNA editing comes in.

RNA editing is like a proofreading process that happens after your DNA's instructions are copied. Instead of just following the recipe exactly, your cells can make tiny changes to the instructions. These changes can help the body adapt to different situations by creating new versions of proteins that might be better suited to certain tasks.

In humans and fruit flies alike, RNA editing prevents autoimmune responses and adjusts protein functions. However, in humans, most editing occurs in non-coding regions, with only a small fraction leading to changes in protein function. In contrast, in flies, the majority of RNA editing events occur in sequences that directly produce proteins.

Given the abundance of RNA editing events that lead to changes in protein-coding sequences in flies, a major challenge is determining which of these thousands of events is biologically important and worth investigating.

Researchers from Bar-Ilan University in Israel have now pinpointed one such event and determined its pivotal role in the sense of smell and social interactions of Drosophila (fruit flies). The findings of their study appear in the journal *Science Advances*.

In selecting the particular editing event to investigate, the research team focused on editing events evolutionarily conserved for millions of years across multiple Drosophila species. They narrowed down their search to a specific event in the GluClα channel likely to have significant functional importance. This event, in which isoleucine is edited to valine, is crucial for the ability of flies to sense odors for social interactions that depend on sensing pheromones, small molecules that allow

communication between individuals.

To test the importance of the site, the researchers used CRISPR technology to abolish RNA editing. This was followed by a battery of behavioral tests which strongly and repeatedly revealed that flies with unedited RNA struggled with their sense of smell and social communication. Flies with the unedited GluClα channel exhibited impaired ability to be attracted to smells of apple juice or alcohol, and to avoid smells that warn them of danger. They also exhibited impaired social interaction capabilities which are necessary for survival and reproduction.

Further analysis pinpointed specific neurons in the brain responsible for processing odors that were affected by the lack of RNA editing. The researchers proposed a model to explain how editing at different locations in the GluClα channel helps it function correctly, and why editing is necessary instead of just constant mutation.

"Our findings highlight how essential RNA editing is for normal behavior," said Prof. Galit Shohat-Ophir, of Bar-Ilan University's Goodman Faculty of Life Sciences, Gonda Brain Research Center and Nanotechnology Institute.

"We were surprised by how strongly and consistently the lack of editing impacted the flies. This underscores just how critical these tiny changes are for the expression of complex behaviors," added Prof. Shohat-Ophir, who led the study with graduate student Hila Zak, in collaboration with Tel Aviv University Prof. Moshe Parnas, Stanford University Prof. Jun Billy Li, and Dr. Yoav Pass, of Bar-Ilan University.

This study highlights the enormous potential and importance of RNA editing in shaping the physiology and behavior of animals. In future research, Prof. Shohat-Ophir hopes to discover how the editing level is

regulated to allow flexibility to respond to environmental changes and internal needs.

**More information:** Hila Zak et al, A highly conserved A-to-I RNA editing event within the glutamate-gated chloride channel GluClα is necessary for olfactory-based behaviors in Drosophila, *Science Advances* (2024). DOI: 10.1126/sciadv.adi9101

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