New genetic editing powers discovered in squid

March 23 2020

The longfin inshore squid, Doryteuthis pealeii, long established as a research organism for fundamental biological studies. Credit: Elaine Bearer

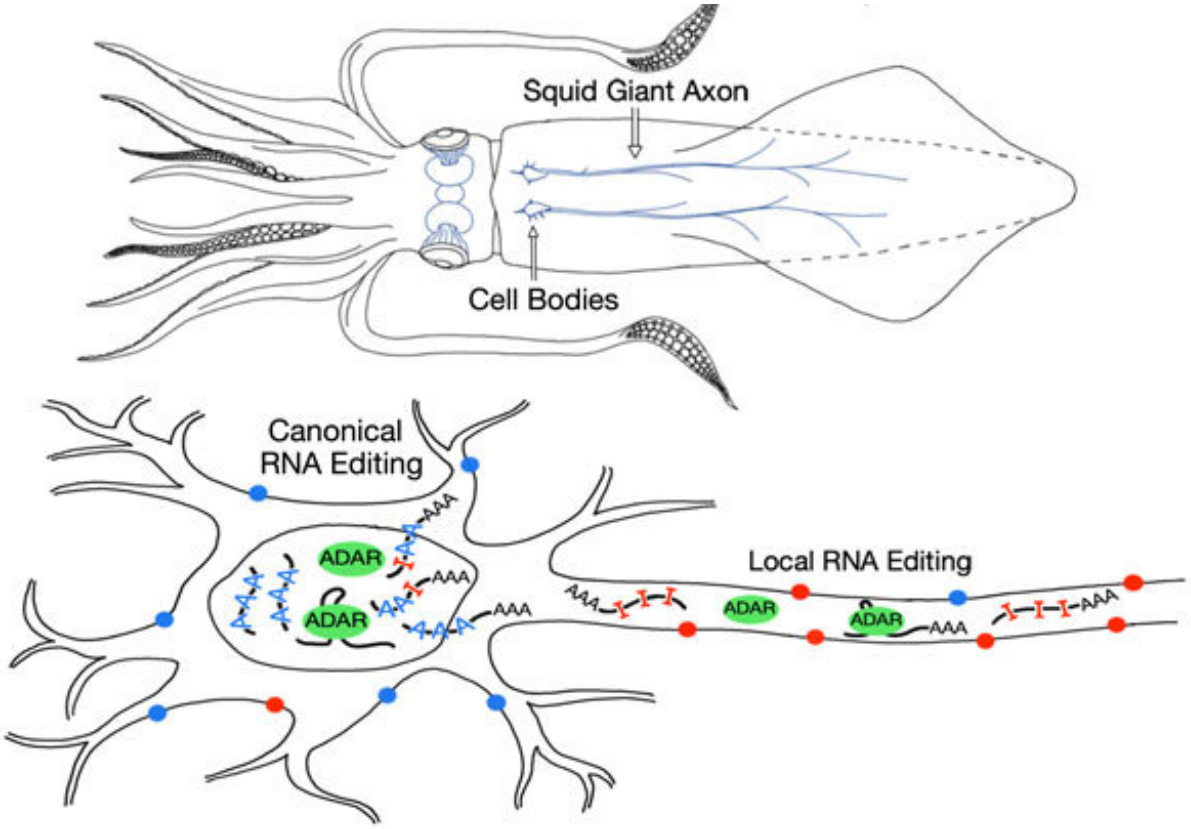
Revealing yet another super-power in the skillful squid, scientists have discovered that squid massively edit their own genetic instructions not only within the nucleus of their neurons, but also within the axon—the long, slender neural projections that transmit electrical impulses to other neurons. This is the first time that edits to genetic information have been observed outside of the nucleus of an animal cell.

The study, led by Isabel C. Vallecillo-Viejo and Joshua Rosenthal at the Marine Biological Laboratory (MBL), Woods Hole, is published this week in *Nucleic Acids Research*.

The discovery provides another jolt to the "central dogma" of molecular biology, which states that genetic information is passed faithfully from DNA to messenger RNA to the synthesis of proteins. In 2015, Rosenthal and colleagues discovered that squid "edit" their messenger RNA instructions to an extraordinary degree—orders of magnitude more than humans do—allowing them to fine-tune the type of proteins that will be produced in the nervous system.

"But we thought all the RNA editing happened in in the nucleus, and then the modified messenger RNAs are exported out to the cell," says Rosenthal, senior author on the present study. "Now we are showing that squid can modify the RNAs out in the periphery of the cell. That means, theoretically, they can modify protein function to meet the localized demands of the cell. That gives them a lot of latitude to tailor the genetic information, as needed." The team also showed that messenger RNAs

are edited in the nerve cell's axon at much higher rates than in the nucleus.



Top, schematic of squid anatomy showing the location of the "giant axon," an unusually large neural projection that partly controls the squid's jet propulsion system, used for very fast movement, attacks and escapes. Below, schematic of a neuron, showing the location of the nucleus where all RNA editing was previously thought to occur, and the axon, where local RNA editing was identified in squid. Credit: From: Vallecillo-Viejo et al, Nucl. Acids Res., 2020.

In humans, axon dysfunction is associated with many neurological disorders. Insights from the present study could accelerate the efforts of biotech companies that seek to harness this natural RNA editing process

in humans for therapeutic benefit.

Scientists from Tel Aviv University and The University of Colorado at Denver collaborated with MBL scientists on the study.

Previously, Rosenthal and colleagues showed that octopus and cuttlefish also rely heavily on mRNA editing to diversify the proteins they can produce in the nervous system. Together with squid, these animals are known for strikingly sophisticated behaviors, relative to other invertebrates.

More information: Isabel C Vallecillo-Viejo et al, Spatially regulated editing of genetic information within a neuron, *Nucleic Acids Research* (2020). DOI: 10.1093/nar/gkaa172

Provided by Marine Biological Laboratory