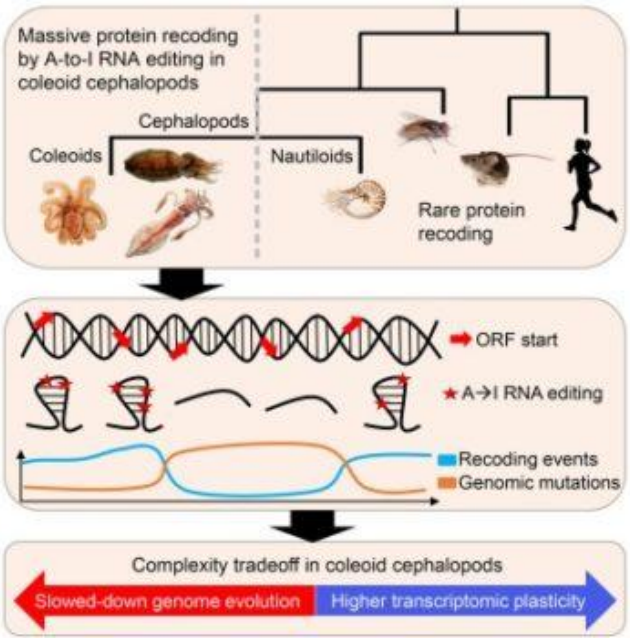
‘Central Dogma’ of Genetics defied by Octopuses and Squids



Genetic information is transmitted relatively faithfully from DNA to RNA, and on into proteins in most of the organisms. But scientists have noted previously that some cephalopods — the class of molluscs that includes octopuses and squid — make extensive use of enzymes to edit their RNA, producing proteins that differ markedly from those encoded by the DNA.

Now the study led by researchers , Joshua Rosenthal at the Marine Biological Laboratory in Woods Hole, Massachusetts, Eli Eisenberg at Tel Aviv University in Israel and their colleagues, have found that RNA editing is particularly common in the behaviourally complex cephalopods (cuttlefish, squid and octopuses) and occurs most frequently in RNA sequences associated with neural function (more than 60 percent of RNA transcripts in the squid brain are recoded by editing, while in humans or fruit flies, only a fraction of 1 percent of their RNAs have a recoding event).The scientists found tens of thousands of evolutionarily conserved RNA recoding sites in this class of cephalopods, called coleoid where the editing is especially enriched in the nervous system, affecting proteins that are the key players in neural excitability and neuronal morphology.

RNA editing in the more primitive cephalopod Nautilus and in the mollusk Aplysia occurs at orders of magnitude lower levels than in the coleoids, they found. “This shows that high levels of RNA editing is not generally a molluscan thing; it’s an invention of the coleoid cephalopods”. In mammals, very few RNA editing sites are conserved; they are not thought to be under natural selection. “There is something fundamentally different going on in these cephalopods where many of the editing events are highly conserved and show clear signs of selection,” says Rosenthal.

The team also discovered a striking trade-off between high levels of RNA recoding and genomic evolution in these cephalopods. The most common form of RNA editing is carried out

by ADAR enzymes, which require large structures (dsRNA) flanking the editing sites. These structures, which can span hundreds of nucleotides, are conserved in the coleoid genome along with the editing sites themselves. Due to the large number of sites, the surrounding conservation greatly reduces the number of mutations and genomic polymorphisms in protein-coding regions.

And the researchers concluded that whereas the other animals evolved through frequent DNA mutations, cephalopods have maintained a more static genome, instead adapting by diversifying their proteins through RNA editing. These animals were suppressing the mutation to maintain recoding flexibility at the RNA level.

Rosenthal and colleagues at the MBL are currently developing genetically tractable cephalopod model systems to explore the mechanisms and functional consequences of their prolific RNA editing.