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Science News

By G.Timokhin

New genetic editing powers discovered in squid

Source: Marine Biological Laboratory (MBL), Woods Hole

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NAR Breakthrough Article

Spatially regulated editing of genetic information within a neuron

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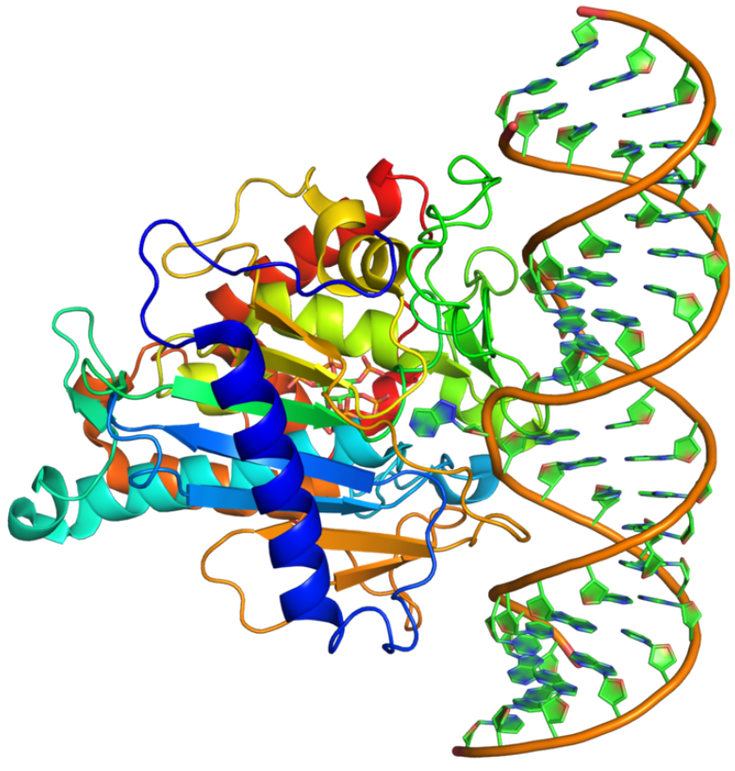
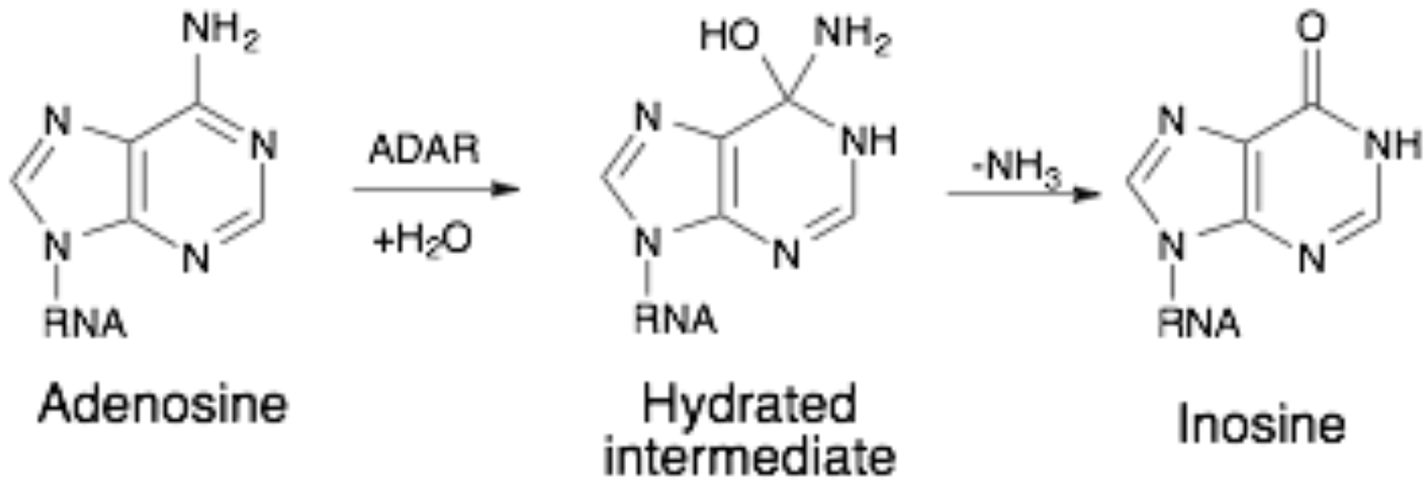
ADAR

Adenosine deaminases acting on RNA (ADAR) are enzymes responsible for binding to double stranded RNA (dsRNA) and converting adenosine (A) to inosine (I) by deamination

Inosine typically mimics guanosine during translation





Adenosine | Hydrated intermediate | Inosine

Unlike other taxa, cephalopods diversify their proteomes extensively by RNA editing

Extensive recoding is specific to the behaviourally complex coleiods

Unlike mammals, cephalopod recoding is evolutionarily conserved and often adaptive

(Eisenberg et al., 2017)

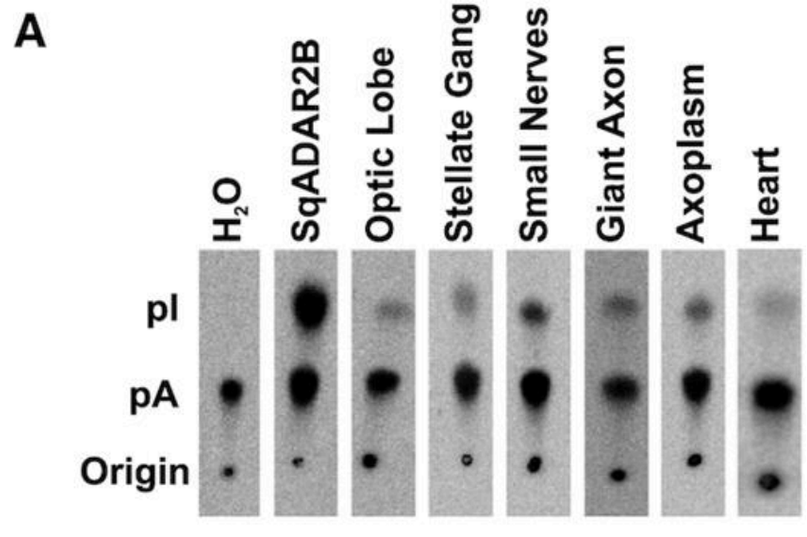
"The coleoid cephalopods use A→I editing to recode proteins at levels that are orders of magnitude higher than any other organism studied to date. The common market squid, for example, recodes about two-thirds of its neural messages by this mechanism and octopus and cuttlefish edit at similar frequencies"(Rosenthal et al., 2020)

ADAR2 is expressed outside of the nucleus in squid neurons

Purified axoplasm exhibits adenosine-to-inosine activity and can specifically edit adenosines in a known substrate.

A transcriptome-wide analysis of RNA editing reveals that tens of thousands of editing sites (>70% of all sites) are edited more extensively in the squid giant axon than in its cell bodies.

These results indicate that within a neuron RNA editing can recode genetic information in a region-specific manner.



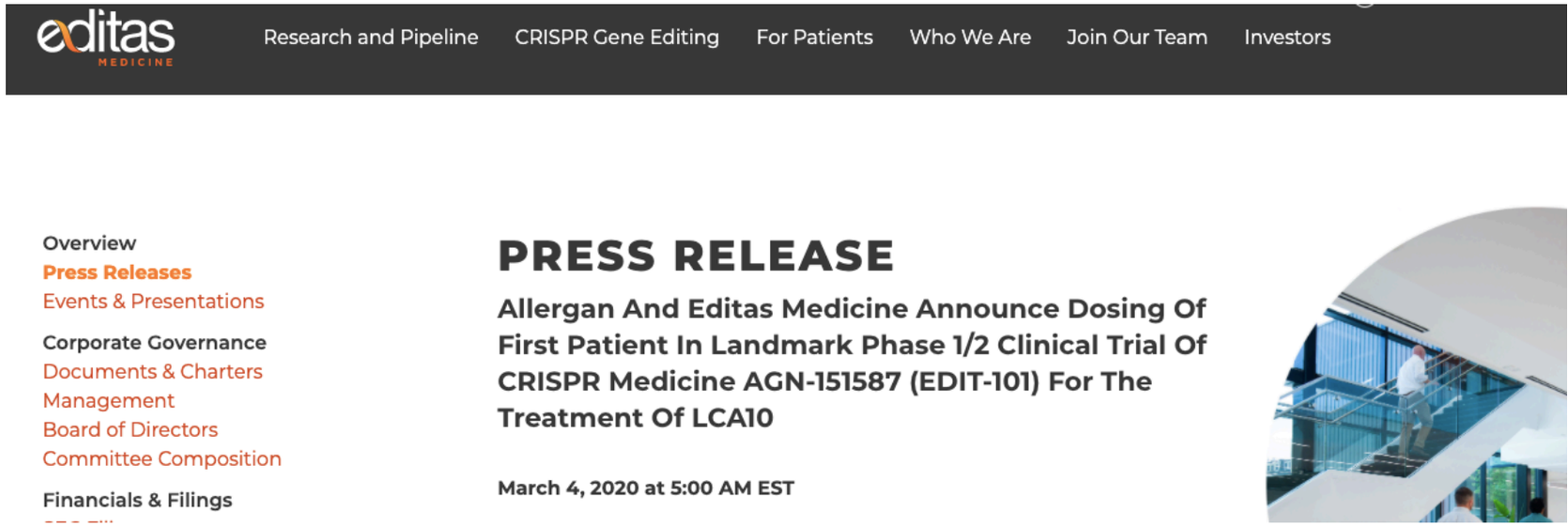
(**A**) Images of thin-layer chromatography plates used to separate radiolabeled adenosine and inosine from dsRNA editing assays with different tissues extracted from *D. pealeii*. Recombinant sqADAR2b was incubated as a positive control and assays with water were performed as negative controls. (**B**) Editing percentages were quantified based on A-to-I conversion; $n = 3 \pm$ standard error of the mean (SEM). AD = sqADAR2b; OL = optic lobe; SG = stellate ganglion; SN = small nerve fibers; GA = giant axon; AP = axoplasm; HE = heart. OL, SG and HE samples contain both nuclei and cytoplasm.

This is the first time that edits to genetic information have been observed outside of the nucleus of an animal cell.

Doctors try 1st CRISPR editing in the body for blindness

Source: Allergan, Editas Medicine

Date: March 4, 2020



The people in this study have Leber congenital amaurosis…

Scientists can't treat it with standard gene therapy — supplying a replacement gene — because the one needed is too big to fit inside the disabled viruses that are used to ferry it into cells.

So they're aiming to edit, or delete the mutation by making two cuts on either side of it. The hope is that the ends of DNA will reconnect and allow the gene to work as it should.

It's done in an hour-long surgery under general anaesthesia. Through a tube the width of a hair, doctors drip three drops of fluid containing the gene editing machinery just beneath the retina, the lining at the back of the eye that contains the light-sensing cells.

The gene editing tool CRISPR has been used inside someone's body for the first time

It may take up to a month to see if it worked to restore vision. If the first few attempts seem safe, doctors plan to test it on 18 children and adults.