A novel way of editing genetic messages

Imagine deciphering a coded message but having no way to trace its origin. Molecular geneticists have faced this frustration ever since the 1986 discovery that cells of many organisms, from protozoans to people, contain extra bits of genetic information that aren't obviously encoded by the DNA in their genes.

The extra information appears in messenger RNA (mRNA). DNA routinely transcribes mRNA molecules to shuttle its message to the cell's protein-synthesis machinery, which translates the message into proteins. But the discovery that extra genetic material subsequently gets added into certain mRNA molecules – a process called RNA editing – has left scientists searching for the DNA-like molecular template that encodes the edited mRNA sequences.

Now, researchers think they have identified the source of the added material. Working with mitochondrial DNA from the protozoan *Leishmania tarentolae,* the team has found evidence that some DNA molecules nestled between genes – and previously considered inactive – serve as templates for a newly recognized class of small RNA molecules that carry out the editing process. The researchers call these RNA molecules "guide RNA" (gRNA).

"RNA editing is a novel mechanism of information transfer between RNA molecules," says Larry Simpson of the University of California, Los Angeles, who coauthored the report in the Jan. 26 CELL. In the mechanism his group proposes, short gRNA molecules form a double-stranded complex with certain mRNA molecules. The gRNA edits the mRNA by specifying the addition or deletion of an RNA building block called uridine. Adenine, uridine, guanine and cytosine are the four building blocks, or bases, that make up RNA.

When DNA transcribes mRNA, the sequence of bases in the DNA leads to a complementary sequence in the mRNA. Scientists have traditionally recognized adenine-uridine and guanine-cytosine as the complementary base pairs in RNA. But in their new model, Simpson's group considered the possibility of a third complementary base pair: guanine-uridine. Though unusual, this pairing has been observed in other types of RNA molecules. Simpson asserts that the failure to recognize guanine-uridine pairing has hindered scientists in their search for missing template.

In RNA editing, wherever a guanine or an adenine occurs on the gRNA side of the mRNA-gRNA complex, a uridine is added to the mRNA sequence, he says. Because this mRNA must be edited before it can get translated into proteins, the editing step essentially regulates protein synthesis, Simpson suggests.

The researchers do not yet know whether their proposed mechanism applies to RNA editing in other organisms and cell types. "It is possible that the RNA-based mechanism could work for other types of RNA editing in plants and humans, but there is no evidence of that," Simpson cautions.

Even so, their report has raised the spirits of scientists puzzled by the editing phenomenon. "It's fabulous," says biochemist Alan M. Weiner at Yale University. "The finding is the beginning of a revolution of something that has driven us all crazy."

Gerald F. Joyce of the Research Institute of Scripps Clinic in La Jolla, Calif., adds, "They clearly have the answer to the big question, which is: Where is the template?"

But another new study hints that the search may not have ended. In the Feb. 1 NATURE, Vladimir Volloch and his colleagues at the Boston Biomedical Research Institute describe their work with the protozoan *Trypanosoma brucei,* which causes African sleeping sickness. Their findings seem to contradict Simpson's. They indicate that the bulk of edited RNA is synthesized *during* rather than after mRNA transcription from a still-unidentified template that produces only edited mRNA. The researchers add, however, that their method may not have been sensitive enough to detect editing taking place *after* mRNA transcription.

Simpson says his team hopes to generate edited mRNA *in vitro* by adding gRNA of a known sequence to synthetic, pre-edited mRNA. This, he told SCIENCE NEWS, would prove that RNA editing takes place in preexisting mRNA molecules.

– C. Decker

Bush holds cautious course on global change

President Bush urged caution in responding to the threat of global warming in an address before an international environmental conference last week, while 10 European nations stressed their desire to begin negotiations quickly toward setting limits on emissions of carbon dioxide.

At the meeting of the Intergovernmental Panel on Climate Change (IPCC) in Washington, D.C., Bush asserted the need to improve scientific knowledge about global change and to consider carefully a range of policy options to protect the global environment.

"Some may be tempted to exploit legitimate concerns for political positioning. Our responsibility is to maintain the quality of our approach, our commitment to sound science, and an open mind to policy options," the President said.

To the disappointment of international environmental groups, Bush did not announce any specific new policies to slow global warming, which can result from the atmospheric accumulation of greenhouse gases such as carbon dioxide and chlorofluorocarbons. In his speech before the IPCC, the President also maintained that environmental policies need not slow economic growth or restrict the free market.

Established in 1988 by the United Nations Environment Program and the World Meteorological Organization, the IPCC is assessing scientific climate data, the likely future impacts of global change and the policy options available to the international community. Its report, due this summer, will serve as a focus for discussions during the Second World Climate Conference in Geneva this fall.

During the IPCC meeting, 10 European delegations urged the world's governments to begin preparatory negotiations that would allow ministers at the Geneva conference to commit the industrialized countries to stabilize emissions of carbon dioxide by the year 2000. Sweden, Austria, Denmark, the Federal Republic of Germany, Finland, France, the Netherlands, Norway, Switzerland and Italy offered the proposal, although the IPCC has no authority to adopt any binding policies.

"We would like to see things happening, to put it simply. That was the essence of it and maybe to put some pressure on some countries that don't seem to be willing to move as fast as we would like to," says Leif Westgaard of the Norwegian Embassy in Washington, D.C.

At an international meeting in the Netherlands last November, many nations supported stabilization by 2005, but the move failed when the United States, the United Kingdom, the Soviet Union and Japan did not commit to the plan (SN: 12/16/89, p. 394).

Several environmental groups argued that governments must move ahead with even more severe measures to curb global warming. "Stabilization of emissions doesn't really respond ultimately to the urgency of the problem. Stabilization of emissions means concentrations will rise at roughly the rate they are rising at now," says Daniel Lashof of the Natural Resources Defense Council in Washington, D.C.

Environmentalists pressed for nations to agree to cut carbon dioxide emissions by 20 percent by the year 2000. Ultimately, Lashof says, emissions must drop by 70 percent in order to stop the atmospheric accumulation of carbon dioxide. Scientists say that even with this step, the planet's surface would still warm due to greenhouse gases already released into the atmosphere over the past few centuries.

– R. Monastersky