necessary western topographic step must have been put in place by tectonics about 20 million years ago. This arose by a combination of broad regional uplift due to upper mantle processes (*11*) and initiation of the Grand Wash Fault at the western edge of the Colorado Plateau. The Colorado River of 20 million years ago poured over this growing step on its way westward.

Each region of the continental crust is uplifted episodically by tectonic forces, but it also adjusts continuously to the unloading caused by erosion itself, rising at a rate slightly less than that of regional denudation [the average rate at which rock is stripped from the region as a whole (*7*)]. The current average denudation rate for the drainage area above Lake Mead is 145 to 160 m per million years (*12, 13*); on the Colorado Plateau itself, it has been measured as 26 m per million years (*13*). The incision rate of 166 to 411 m per million years found by Polyak *et al.* in the eastern Grand Canyon exceeds both these estimates. This means that uplift there was too fast to have been driven by erosion alone. Tectonic forces must have contributed in the past and possibly continue to do so today.

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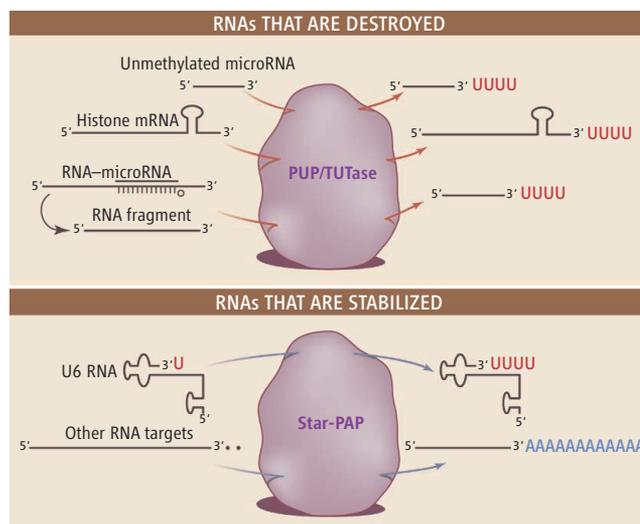
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MOLECULAR BIOLOGY

A Tail Tale for U

Enzymes add strings of uridine or adenosine to control RNA stability.

Marvin Wickens and Jae Eun Kwak

Nothing we learn about the ribonucleic acid (RNA) world should surprise us any more. RNAs that are destroyed just after synthesis, or salvaged from cellular scrap heaps, or that regulate transcription—the process by which RNAs themselves are made—already are commonplace. Yet surely a few things in this fluid world are fixed, such as the string of adenosine bases [poly(A) tail] that is added to the end of eukaryotic messenger RNAs (mRNAs), the templates transcribed from DNA that encode proteins. Now even this terra firma is unstable. Recent work identifies enzymes that synthesize polyuridine [poly(U)], and shows that poly(U) tails not only exist on certain mRNAs, but can control mRNA decay.

Many RNAs receive extra nucleotides at their 3′ ends after transcription. These "tails" are not copied from DNA, but are synthesized de novo. Poly(A) is the best known, contributing to the stability and export of mRNAs and their translation to proteins. However, U's are added to the ends of guide RNAs that function in RNA editing (*1*) and to certain microRNAs (*2*) and small nuclear RNAs (*3*).

Several enzymes that catalyze "tailing" belong to a superfamily of DNA polymerase β–like nucleotidyl transferases (*4*).

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RNAs THAT ARE DESTROYED
Unmethylated microRNA
Histone mRNA
RNA–microRNA
RNA fragment
PUP/TUTase
UUUU
UUUU
UUUU

RNAs THAT ARE STABILIZED
U6 RNA — 3′ U
Other RNA targets
Star-PAP
3′ UUUU
3′ AAAAAAAAAAAA

Dual-personality enzyme. Nucleotide polymerases can add a poly(U) tail (PUP/TUTase activity) or poly(A) tail (Star-PAP activity) to specific RNAs to control their degradation or stability.

This includes poly(A) polymerases (PAPs), which add poly(A) to mRNAs. Recently, a new family of enzymes that add poly(U) was identified (*5*). These poly(U) polymerases (PUPs) are widespread, from yeast to humans. Another member of the same superfamily called terminal uridylate transferase (TUTase) adds short U tails [oligo(U)] to a noncoding RNA, U6 (*1, 6*). Although PUPs and TUTases diverge substantially in sequence, their functions may overlap.

A new PUP-related enzyme identified by Mellman *et al.* (*7*) is particularly provocative because it adds U's to one type of RNA and A's to others. Initially, it was shown that the mammalian enzyme U6 TUTase adds one to three U's to the end of U6 RNA, a small RNA involved in RNA splicing (*6*). Mellman *et al.* show that the same enzyme is a divergent PAP, dubbed Star-PAP. Star-PAP is nuclear, and associates with proteins that cleave the 3′ end of precursor mRNAs, implying an alternative mRNA processing machine. Candidate mRNA targets have been identified and include many involved in the oxidative stress response.

Star-PAP also binds to phosphatidylinositol 4-phosphate 5-kinase α, an enzyme that generates a specific phosphoinositide, phosphatidylinositol 4,5-bisphosphate. Remarkably, the same phosphoinositide stimulates Star-PAP activity. Thus, perhaps in response to stress, the kinase produces a small-molecule signal (a phosphoinositide) that specifies the maturation of targets mRNAs. Another enzyme that targets RNA, ADAR2, is regulated by a different phosphoinositide (*8*). Very likely, small molecules regulate other enzymes that act on RNA, but have escaped notice.

Like Star-PAP, other PUPs may be dual-purpose. For example, in the yeast *Schizosaccharomyces pombe*, CID1 can add either U's or A's to RNAs in vitro (*5, 9*). Although CID1 and other PUPs synthesize only poly(U) in the cell (*5*), their nucleotide preference could be modulated by small molecules or vary with the targeted RNA. With Star-PAP, the phosphoinositide could trigger such a switch in activity. In vivo studies are needed to test this notion decisively, though detecting RNAs that have received poly(U)

will be challenging if they are unstable.

New functions for poly(U) are emerging. The tail can be added to mRNAs to trigger their decay. mRNAs that direct the synthesis of histones—the major protein constituents of chromatin—during the cell division cycle are rapidly degraded once DNA replication is completed or blocked. Intermediate mRNAs in this decay process often have poly(U) tails of 8 to 10 residues (10). Small interfering RNAs directed against two candidate PUP enzymes blocked this degradation, implying that poly(U) addition is essential for their decay. Also, in *S. pombe*, a PUP adds poly(U) to actin mRNA, though its effect on turnover is unknown (9).

A poly(U) tail may enhance degradation by stimulating removal of the mRNA's 5′ cap structure, a key step in mRNA turnover. Poly(U) tails enhance "decapping" in a cell-free system (11). Likely, the tails bind the Lsm protein complex, which associates with decap-

ping factors (11, 12). Indeed, depletion of Lsm1 inhibits histone mRNA turnover (10).

Addition of uridines probably has diverse consequences, including RNA stabilization (6); yet this modification often occurs on an RNA's road to ruin (see the figure). Aberrantly unmethylated microRNAs in the plant *Arabidopsis thaliana* are modified with oligo(U) and destroyed (2). Fragmentation of mRNA by microRNAs is accompanied by the addition of oligo(U) to the pieces before they disappear (13). The most common mRNA decay pathway involves association of the Lsm complex to the mRNA after poly(A) removal. Even this route may rely on evanescent, short oligo(U) because the Lsm complex preferentially binds 3′-terminal uridine tails.

The discovery of poly(U) tails on mRNAs opens unexplored territory in the RNA world. Dual-personality enzymes could switch an mRNA's fate from life to death simply by a

change in the nucleotide they accept. Others may well wait in the wings, along with proteins that target specific RNAs, or remove the tails. Count on new roles for poly(U), an expanding list of RNAs that receive it, and more startling enzymes that put it on and take it off.

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BEHAVIOR

Punishment and Cooperation

Herbert Gintis

Data from economic games show that the effectiveness of punishment in fostering cooperation varies greatly from society to society.

Even champions of modern society agree that it involves a loss of community (based on family and ethnic ties) and an expansion of civil society, with emphasis on the more impersonal interactions among individuals with minimal social ties. For two centuries, this dichotomy has anchored our understanding of modern Western society, applauded by its defenders as the fount of freedom (1), yet identified as the source of inequality (2), the decline of community (3), the destruction of the environment (4), and the impotence of grassroots political action (5). On page 1362 of this issue, Herrmann et al. (6) report their discovery that university students in democratic societies with advanced market economies show different social behavior from that exhibited by students in more traditional societies based on authoritarian and parochial social institutions. Their results suggest that the success of democratic market societies may depend critically on moral virtues as well as material interests, so the depiction of civil society as the sphere of "naked self-interest" is radically incorrect.

The standard view holds that human nature has a private side in which we interact morally with a small circle of intimates and a public

side in which we behave as selfish maximizers. Herrmann et al. suggest that most individuals have a deep reservoir of behaviors and mores that can be exhibited in the most impersonal interactions with unrelated others. This reservoir of moral predispositions is based on an innate prosociality that is a product of our evolution as a species, as well as the uniquely human capacity to internalize norms of social behavior. Both forces predispose individuals to behave morally even when this conflicts with their material interests.

These results are the latest to document a principle of reciprocity according to which people are more willing to sacrifice private gain for the public good as the cost of the sacrifice decreases and as expectations of the extent that others will sacrifice grows. In addition, individuals embrace such character virtues as honesty, trustworthiness, consideration, and loyalty (7). Of course, these moral predispositions moderate rather than eliminate considerations of self-interest and loyalties to kith and kin.

Suggestive evidence for the principle of reciprocity comes from daily life. For instance, political democracy has frequently been attained through popular collective action. Voting in elections is widespread despite its being personally time consuming, and the

benefits are purely public (a single vote can change an electoral outcome only with infinitesimal probability). Moreover, citizens in democratic societies often vote to give substantial sums to charity, and to approve of poverty relief, although these measures increase the tax burden for the average voter.

Experimental evidence for reciprocity comes from behavioral game theory, which uses economic games in which subjects make choices under varied social conditions. For instance, Herrmann et al. employ a public goods game in which each of four anonymous subjects is initially given 20 tokens, and each is told he can place any number of these tokens in a public account. The tokens in the account are multiplied by 1.6 and the result divided evenly among the four. At the end of the experiment, the tokens are exchanged for real money.

In this game, each individual helps the group most by placing his 20 tokens in the

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