serendipitous observations during studies on anti-sense RNA. What might be the normal purpose of this irreversible process? The most obvious answer might be an antiviral defence mechanism. All RNA viruses have to go through a dsRNA intermediate in their life cycle. Although it is well established that one general defence response triggered by the dsRNA form is the induction of interferon, the unwinding and irreversible modification of RNAs that are in a dsRNA form could complement the interferon effects. But does this in fact happen?

It is conceivable that the footprints of an antiviral dsRNA unwinding/modifying activity may have been left with unexpected and disastrous consequences, and may even have caused a human disease. Measles virus, a member of the paramyxovirus-morbillivirus family, has a negative-stranded RNA genome that is transcribed in the cytoplasm by the virion RNA transcriptase into a series of positive-strand mRNAs. In very rare cases of measles virus infection, a persistent infection occurs that is thought to involve defects in functions related to viral assembly, but not to RNA replication. This can lead to subacute sclerosing panencephalitis (SSPE), a progressive disease of the central nervous system.

Recently, Cattaneo *et al.*¹⁰ reported nucleotide-sequencing studies on cloned mRNAs isolated from autopsy material of SSPE brain. In one case they found that a discrete measles virus mRNA, whose protein product (M protein) is essential for virus assembly, has more than 50 per cent of its U residues changed to C. Although biased hypermutation caused by infidelity of the viral RNA transcriptase while transcribing only the M gene cannot be excluded as a mechanism for this¹⁰, it now seems plausible that the establishment of the persistent infection that led to SSPE results from the newly described dsRNA unwinding/modifying activity. If, during transcription of the viral genome, the M gene mRNA fails to leave the template, the dsRNA unwinding/modifying activity could change the A residues on the template RNA to I. In the next round of transcription of mRNA these I residues are copied to C residues. This two-step conversion mechanism could explain the extensive U to C changes found in the mRNA. It should be emphasized that this is not the sole explanation for persistent infections of measles virus. But the strong mutagenic potential of the dsRNA unwinding/modifying activity may have far-reaching consequences.

Another possible function of this novel activity could be its capacity to change specific RNA molecules, or groups of RNA molecules, including mRNAs. This could be accomplished by expression of complementary RNAs (such as small-nuclear RNAs) either to specific regions

within introns of pre-mRNAs, which could lead to alternative splicing patterns, or by modifications within the exons to bring about changes in the coding specificity. For example, a complementary small RNA that base-pairs to a region of an intron of a pre-mRNA which specifies its splicing pattern could stimulate the dsRNA unwinding/modifying activity to alter the relevant sequence such that it alters its normal splicing pattern. It is also possible that the activity found so far is merely one of many such activities and that other related ones with greater specificity lead to changes such as that found in the apolipoprotein B mRNA^{1,2}. Perhaps the activity is a general way of ensuring that segments of RNA that have the tendency to form double-stranded structures (intra- or inter-molecular) are maintained in single-stranded form. Should this not be reason for those in the field to look for inosine in their RNAs?

What could regulate dsRNA unwinding/modifying activity and prevent it from modifying most RNAs in the cell? Two general categories of regulation can be considered. First, there may be specific regulatory components that interact with it but which were separated from it during fractionation. Second, there probably exist activities that can counter the unwinding component of the activity, such as annealing-promoting proteins and proteins that block and protect regions of dsRNA from dissociation. A potent annealing activity has recently been described in nuclear extracts¹¹. Furthermore, RNA molecules exist in cells as RNA-protein complexes with RNP proteins. The recent finding of a complex assortment of RNA-binding proteins in pre-mRNA RNP complexes is an illustration of the abundance and diversity of RNP proteins¹². Many of them, being RNA-binding proteins¹², can function in unwinding and annealing of RNA molecules, and can bind to specific RNA sequences¹³, perhaps protecting them, and thus decisively influence RNA structure. Taken together with the sequence of the RNA itself, the interplay among all these factors will determine the structure and thereby the function of RNA in the cell. □

1. Chen, S.-H. *et al.* *Science* **238**, 363-366 (1987).
2. Powell, L.M. *et al.* *Cell* **50**, 831-840 (1987).
3. Feagin, J.E. *et al.* *Cell* **53**, 413-422 (1988).
4. Thomas, S.M. *et al.* *Cell* **54**, 891-902 (1988).
5. Bass, B.L. & Weintraub, H. *Cell* **55**, 1089-1098 (1988).
6. Bass, B.L. & Weintraub, H. *Cell* **48**, 607-613 (1987).
7. Rebagliati, M.R. & Melton, D.A. *Cell* **48**, 599-605 (1987).
8. Wagner, R.W. & Nishikura, K. *Molec. cell. Biol.* **8**, 770-777 (1988).
9. Abramson, R.D. *et al.* *J. biol. Chem.* **262**, 3826-3832 (1987).
10. Cattaneo, R. *et al.* *Cell* **55**, 255-265 (1988).
11. Munroe, S.H. *EMBO J.* **7**, 2523-2532 (1988).
12. Piñol-Roma, S. *et al.* *Genes Dev.* **2**, 215-227 (1988).
13. Swanson, M.S. & Dreyfuss, G. *EMBO J.* **7**, 3519-3529 (1988).

Robert A. Lamb and Gideon Dreyfuss are in the Department of Biochemistry, Molecular Biology and Cell Biology, Northwestern University, Evanston, Illinois 60208, USA.

Daedalus

Fictitious fat

As many would-be slimmers know, the body has a preferred weight which it defends stubbornly. Even if forced to unload fat, it does so in a specific sequence, which (as in the case of the dreaded 'pear-shape syndrome') may not correspond to the desires of the slimmer. An adult body has a fixed number of fat cells; a successful slimmer succeeds in emptying some of them, while others nearby remain full. This, says Daedalus, makes good chemical sense. A droplet of fat in a cell is potentially metastable. If metabolic demand begins to shrink it a bit, its radius will decrease, its internal pressure will rise, its free-energy balance will shift towards further shrinkage, and the process will accelerate until the droplet is completely metabolized. So a fat cell can have only two stable states, full and empty. It is in fact a digital information-storage element. And this, says Daedalus, is how the body knows how heavy it is. Even within a fat deposit, the cells fill up in a preferred sequence, and it need only record the position of the currently active cell to know how far the process has got. This 'full up to here' signal is presumably relayed by the nerve connection from the cell.

This theory explains the digital accuracy with which some people maintain a steady weight despite their chaotic eating habits. It also suggests a new, powerful, and effortless way to lose weight. You merely generate a false 'full up to here' signal, suggesting to the body that a specific fat deposit is far fuller than it really is. It will then shed fat from that deposit, in an effort to restore the proper apparent loading.

So DREADCO volunteers are being gorged on a wildly calorific diet, and subsequently starved back to normal weight, while an NMR tomographic-imaging system maps the preferred sequence of filling and emptying of their fat cells. Daedalus will thus locate the last cell to be filled in each fat deposit. A false 'full up to here' signal from this cell would imply that the deposit is utterly full. So mild electric shocks at this exact location should induce rapid and effortless slimming. Indeed, a commercial shock-slimming system, claimed to work by stimulating the muscles, probably owes its sporadic success to this effect. But DREADCO's version will launch its false signals with reliable accuracy, giving far more dramatic results. Conversely, a false signal launched from the first-filled cell of a fat deposit will cause that deposit to gain weight.

Thus DREADCO's Programmed Electric Body Sculpture will reshape the user's fat deposits under full control. The pear-shape syndrome will be banished forever!

David Jones