no means established that "decadal variability" is sui generis, created by mechanisms that single out the decadal band for special treatment (*9*). If not, then the hunt for the decadal time setter will prove fruitless. The climate physics behind all of the variability must work in other ways. One clue is that many dynamical systems with nonlinearities or very large dimension also vary at all possible frequencies.

Both the PDO and the NAO extend into the tropics. It has been suggested that decadal variability in the tropical Pacific is induced from mid-latitudes through oceanic pathways, but this has now been convincingly ruled out by studies showing that observed variability in the tropical ocean is accounted for by low-latitude winds (*10*). It remains possible that the low-latitude wind changes are triggered from mid-latitudes, but the evidence for this is not strong. On the other hand, the same coupled ocean-atmosphere physics that generates the interannual El Niño cycle can generate variability at periods longer than interannual (*11*). Furthermore, the El Niño example, supported by much theoretical work and model experiments, demonstrates that variations in the tropics can generate variations at all latitudes. Linsley *et al.* (*1*) observe that the low-frequency variability in their Rarotonga record is related to variations in the North Pacific. This points to a tropical source, a suggestion made in some earlier studies of the shorter instrumental record (*12*). The time series shown in the second figure strengthens their case. A proxy record for SST anomalies in the central equatorial Pacific constructed from tree ring data in the Americas (*13*) correlates at the 98% significance level with the Rarotonga record over the common period 1739–1978 (see the second figure).

It would be impossible to establish statistical significance with the short records derived solely from instrumental data. With a number of well-placed, reliable proxy records several centuries in length and with annual resolution or better, progress in understanding decadal variability will accelerate. Even then, however, there is no guarantee that useful predictions will prove to be possible.

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PERSPECTIVES: MOLECULAR BIOLOGY

Unwinding RNA Silencing

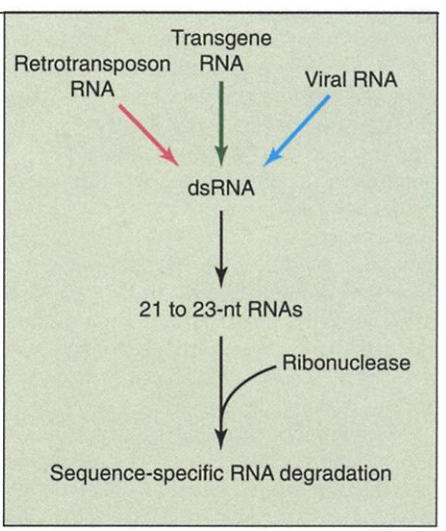
David C. Baulcombe

Eukaryotic cells have developed an elegant defense system to eliminate unwelcome foreign RNA molecules. This defense system is variously described as posttranscriptional gene silencing in plants, RNA interference in vertebrates and invertebrates, and quelling in fungi (*1*). Work in the worm and fruit fly suggests that RNA silencing may protect the genome from mobile DNA elements called retrotransposons that are derived from viruses. These elements produce an RNA intermediate that enables them to move about within the genome and to inactivate essential genes (*2*). In plants, RNA silencing protects plant cells by degrading the nucleic acid of RNA viruses (*3*).

The molecular machinery of RNA silencing is remarkable in that it targets not only foreign RNA but also other RNAs in the cell that have a similar sequence to the foreign RNA. Once initiated, RNA silencing apparently continues to suppress the expression of RNA species even after the original foreign RNA has been eliminated. Exactly how foreign RNAs are silenced is still unclear, but a report by Wu-Scharf *et al.* (*4*) on page 1159 of this issue is beginning to shed light on the mystery. These investigators describe a mutant form of the green alga *Chlamydomonas* in which RNA silencing is abrogated. They show that the affected gene in the mutant form, called *Mut6*, normally encodes an RNA helicase that has the capacity to unwind double-stranded RNA (dsRNA) such as that found in many RNA viruses.

Wu-Scharf and colleagues engineered wild-type and *Mut6* forms of *Chlamydomonas* to carry a synthetic gene (transgene) that conferred resistance to the antibiotic spectinomycin. When grown on medium containing this antibiotic, wild-type algae soon died because their RNA silencing mechanism prevented expression of the transgene, whereas *Mut6* algae (in which RNA silencing was shut down) grew robustly. What is more, the loss of RNA silencing in *Mut6* mutant cells resulted in an increase in the movement of the retrotransposons TOC1 and *Gulliver* within the algal genome. This demonstrated that the effect of a mutated *Mut6* gene is similar to the loss of the *Mut7* gene in worms, which is required for silencing of retrotransposon and transgene RNA (*2*).

What is the cue for activation of RNA silencing? In some instances, the double-strandedness of RNA may be involved because, in worms and fruit flies, an effective means of activating RNA silencing is to directly introduce dsRNA into the cell (*5*). However, when the foreign nucleic acid is made of DNA, as is the case for retrotransposons and transgenes, it is possible that the cell detects misprocessing or premature termination of the single-stranded RNA transcribed from the foreign DNA. Wu-Scharf *et al.* show that aberrant RNAs—from the spectinomycin-resistance transgene, the TOC1 retrotransposon, and the



Silencing RNA. Eukaryotic cells have several RNA silencing mechanisms. These detect and degrade foreign RNAs originating from viruses, retrotransposons, or transgenes (colored arrows). In one mechanism, foreign double-stranded RNAs (dsRNAs) such as those from viruses are processed into short 21- to 23-nucleotide sequences. These short sequences activate ribonuclease enzymes and guide them to the foreign RNA (and cellular RNAs of similar sequence), which is then degraded.

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mutated *Mut6* gene—are present only at low levels in wild-type *Chlamydomonas* but are abundant in the *Mut6* algae.

The molecular basis of the recognition of aberrant single-stranded RNAs is not well understood. However, it is likely that an RNA-dependent RNA polymerase plays an important part by converting the aberrant single-stranded RNA into a double-stranded form. In the plant *Arabidopsis*, an RNA-dependent RNA polymerase encoded by the *Sde1* locus is required for the induction of RNA silencing by a transgene. This enzyme is not required when RNA silencing is activated by viruses that replicate their nucleic acid through a dsRNA intermediate (*6*).

The core of the RNA silencing mechanism, irrespective of whether the foreign RNA is single- or double-stranded, is likely to be the processing of dsRNA into short 21- to 23-nucleotide segments (see the figure) (*7*, *8*). These short RNA species are thought to be incorporated into a ribonuclease (RNase) complex (which is now being characterized in fruit fly extracts) (*9*). The current thinking is that the short RNA species form Watson-Crick base-paired structures within the complex that guide the RNase to the target molecules (foreign dsRNA and cellular RNAs of similar sequence) in the cell, which are then degraded. If true, this model would provide an explanation for why introduction of a foreign RNA into a cell results in degradation not only of that RNA but also of other RNAs with a similar nucleotide sequence (*10*).

The RNA helicase encoded by the *Mut6* gene is similar to the PrP16 protein of human cells that is necessary for the splicing of messenger RNAs (mRNAs) after transcription. It also resembles the worm protein MOG-1, which helps to destabilize an RNA (*fem-3*) that promotes development of male reproductive organs. MUT6 is the second RNA helicase–like protein to be implicated in RNA silencing. Just last month, Domeier *et al.* reported that the worm *smg-2* gene encodes a helicase required for persistent RNA silencing (*11*). SMG-2 and its close homolog in yeast, UPF-1, are necessary for degradation of nonsense mRNAs containing premature stop codons.

SMG-2 is a helicase of superfamily I, most members of which are encoded by RNA viruses, whereas MUT6 is a member of the DEAH-box helicase superfamily II (*12*). Differences between SMG-2 and MUT6 make it unlikely that these proteins operate at the same stage of RNA silencing. However, the involvement of both of these proteins in RNA silencing does suggest that this process is part of the normal molecular network that regulates RNA processing and stability in eukaryotic cells. This network is distinct from the well-characterized cellular machinery that governs the transcription of DNA into RNA.

One reason for the intense interest in RNA silencing (*1*) is that this process is apparently unique to eukaryotic cells. Now, with the discovery of proteins in the RNA silencing pathway (*4*, *13*) that are similar to proteins in other pathways regulating RNA, it is likely that RNA silencing is merely a variation on a well-established cellular theme. But even if it is, for the true RNA connoisseur, there is genuine interest in a process that borrows known protein components to carry out unknown reactions. Whether one is a connoisseur or not, there is no question that the report by Wu-Scharf *et al.* provides a tantalizing clue that should facilitate the unwinding of RNA silencing.

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PERSPECTIVES: CLIMATE

A New Route Toward Limiting Climate Change?

Steven J. Smith, Tom M. L. Wigley, Jae Edmonds

The upcoming sixth meeting of the Conference of the Parties to the Framework Convention on Climate Change (FCCC) from 13 to 24 November in The Hague has refocused attention on climate change policy. The debate has recently been stimulated by Hansen *et al.* (*1*), who have suggested an "alternative scenario" for mitigating climate change. In their proposed mitigation strategy, the increase in carbon dioxide (CO_2) concentration over the next 50 years is limited to an additional 75 parts per million by volume (ppmv) (*2*), equivalent to a radiative forcing increase of 1 W/m^2. (Radiative forcing is the energy imbalance caused by changes such as rising atmospheric CO_2 concentrations. A net positive forcing will cause a warming.) So far, this is rather traditional. But their strategy departs from previous ideas by proposing to enhance aerosol cooling and to limit the total forcing from non-CO_2 greenhouse gases, including tropospheric ozone, to today's level by 2050. The proposed Kyoto Protocol already includes non-CO_2 greenhouse gases such as methane (*3*), but Hansen *et al.*'s inclusion of ozone and aerosol effects—both of which are short-lived local and regional air pollutants—would be a new addition to global policy. Is this proposal viable?

To evaluate the plausibility of any climate policy, one must first analyze reasonable baseline scenarios from which the policy is meant to depart. Such scenarios represent future demographic, social, economic, technological, and environmental developments that may occur in the absence of a dedicated climate policy. The most up-to-date scenarios are those in the Intergovernmental Panel for Climate Change (IPCC) Special Report on Emissions Scenarios (SRES); they represent a wide range of possible future emissions paths (*4*). The estimated change in radiative forcing over 2000 to 2050 ranges from 1.5 to 3.7 W/m^2 from the entire set of SRES scenarios; CO_2 is responsible for 1.1 to 2.7 W/m^2 depending on the scenario (*5*).

The baseline from which the Hansen *et al.* policy would be easiest to implement is the relatively optimistic SRES B1 scenario family. The B1 family assumes low population growth and, as noted by Hansen *et al.*, "improved energy efficiency and a continued trend toward ... increased use of gas instead of coal" [p. 9878 (*1*)]. Even in the B1 family with its optimistic assumptions, the CO_2 forcing increase ranges from 1.1 to 2.2 W/m^2. Meeting the net 1 W/m^2 forcing target of Hansen *et al.* (*1*) is thus likely to require some, possibly substantial, efforts (*6*). Even larger efforts may be required if future developments follow one of the other SRES scenarios.

In addition to limitations in CO_2 forcing, the largest potential forcing decrease in the Hansen *et al.* strategy would result from changes in aerosol composition. The domi-

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