clearly poor-quality applications. Although we are gratified that the success rate of unamended unsolicited R01 applications has increased over time, we remain committed to and still advocate funding half of peer-recommended applications. A doubling of the NIH budget over 5 years, as initiated by the 15% rise provided for FY 1999, should boost the success rate to more appropriate levels.

For renewal requests (Type 2), NIH states that 49% have been funded in FY 1998 without revision, compared with 37% in FY 1994. However, these research investigations have previously passed stringent peer review and are in full operation, and now 51% are being interrupted or terminated.

Because only limited time may have been available to achieve publishable results, the discontinuation of such programs, after the low success rate for first-time submissions, can cause major disruptions of research. Delays in funding can stop momentum, break up highly specialized teams of scientists dependent on uninterrupted support, and slow attainment of scientific breakthroughs. The fiscal hiatus has destroyed professional careers; lack of funding has led to denial of tenure (*3*) and academic dismissal. We need more of our well-trained professional talents to continue their scientific productivity. Desirability of a scientific career should not be diminished in this way if we wish to recruit outstanding new candidates. For all these reasons, we urge that sufficient funds be provided to minimize all-too-costly interruptions in funding, with increasing availability of bridge support, for Type 2 renewal applications, especially for those close to the pay line.

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References and Notes

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Overlooked Control

A serious technical oversight in some molecular regulation studies is occurring at an increasing rate. The tetracycline (tet)-inducible gene expression system has become a commonly used approach to experimenter-controlled expression of genes for functional evaluation in mammalian cells (*1*). There are two controls required for sound interpretation of cellular effects that occur when a "tet-inducible" gene is activated. The first control is the off-condition for the evaluated gene. The second is the on-condition for control cells derived with the tet-repressor–VP16 transactivator protein, but with an empty tet-operator vector. Invariably, this essential control is omitted. Of 12 surveyed recent reports using tet-inducible systems (*2*–*13*), only one reported a control of this type (*8*).

Removal of tetracycline or addition of doxycycline to induce test gene expression may appear to be otherwise innocuous events. However, they unleash the activity of a potent gene transactivator (*14*). Although the tet-repressor–VP16 fusion protein has a high affinity for the tet-operators, nothing prevents it from binding at other gene loci

either nonspecifically or specifically by means of operator-like genomic sequences. Such binding events will sometimes interfere with normal gene expression and lead to cellular disturbances that will be erroneously attributed to expression of the evaluated gene. This caveat is particularly applicable to evaluations of genes that are thought to function as growth suppressors (for example, *2, 5, 6, 9–11, 13*).

Empty-vector cell lines serve as excellent controls for general cellular effects of the transactivator fusion protein. Of course, no single cell line can control for idiosyncratic induction effects that may occur in a given tet-inducible cell line. This shortcoming highlights the general importance that final conclusions regarding the function of an evaluated gene are based on polyclonal analyses or on at least two independently derived tet-inducible cell clones. This is another often overlooked consideration (*2, 4, 5, 11–13*). This requirement will safeguard against erroneous conclusions based on responses that depend on the integration site of the tet-operator test gene construct.

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CORRECTIONS AND CLARIFICATIONS

In "Solar homes for the masses" by Alexander Hellemans (Energy, 30 July, p. 679), the first sentence of the third paragraph contained an error. It should have read, "Amersfoot gets much less sunshine than the world average of 1360 watts per square meter."

In the Report "*Equatorius*: A new hominoid genus from the Middle Miocene of Kenya" by S. Ward *et al.* (27 Aug., p. 1382), the first full paragraph of the second column on page 1383 should have begun, "**Etymology**: The name reflects the proximity to the equator of all localities from which the genus has been recovered. **Type species**: *Equatorius africanus* (Le Gros Clark and Leakey, 1950)." The reference referred to is W. E. Le Gros Clark and L. S. B. Leakey, *Q. J. Geol. Soc. London* **105**, 260 (1950).