highest biological importance and to direct development to less sensitive areas. Ample evidence exists to suggest that protection is necessary: Where there is demand for resources, those resources are likely to be lost to land conversion or overuse if they are not actively protected (*2*).

Bhagwat *et al.* also suggest that current differences between parks and their surroundings might reflect preexisting differences, although they present no evidence to support their claim. It would not be true for parks created in remote wilderness areas, for example, because their surroundings would also be wilderness. Further, our finding that natural vegetative cover increased in 40% of parks after establishment suggests that these areas faced threats before park establishment and that the park subsequently mitigated these threats enough to allow recovery.

Concerning study design, respondents had little incentive to overestimate effectiveness. We guaranteed anonymity and agreed to publish only aggregate findings that could not be linked to any particular protected area. In this context, respondents' "vested interest in promoting [park management] effectiveness" would seem best served by providing accurate information, which could in turn provide them with useful findings to guide management. Lack of bias is suggested by the fact that many managers reported that their parks were effective against some threats, but ineffective against others. Regarding the IUCN study mentioned by Bhagwat *et al.*, despite broad differences in methodology, the conclusions of both studies are in fact similar concerning effectiveness. Both show that protected areas face high degrees of threats, and both found that protected areas maintain ecosystems of high value for conservation.

In conclusion, although parks are only one of several conservation options, our study clearly demonstrates that they have been an effective long-term strategy against a range of threats. These findings suggest that increased support for existing parks, and creating new ones, should remain a central focus of tropical conservation efforts.

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References and Notes

1. For a more technical treatment of some of these issues, please also see the Technical Comment exchange with J. K. Vanclay, available at www.sciencemag.org/cgi/content/full/293/5532/1007a
2. M. E. Soulé, M. A. Sanjayan, *Science* **279**, 2060 (1998).

In Defense of Antisense

IN HIS ARTICLE "A FASTER WAY TO SHUT DOWN genes" (News of the Week, 25 May, p. 1469), R. John Davenport describes a promising technique called RNA interference for selectively silencing genes in a range of organisms. But in comparing the new approach to antisense methods, he makes a false assertion: "Fifteen years ago, antisense methods for gene silencing and gene therapy offered similar hopes, but that has been largely a bust."

Like any new method, antisense has faced significant and complex methodological and practical challenges since the first useful demonstration of this method in 1978. Although important issues remain, problems such as drug stability, deliverability, and targetting have been significantly addressed, if not solved. As evidence for these points, there are numerous successful companies that have

been built partially or completely on antisense technology. Several have antisense drugs in the clinical pipeline that treat, for example, devastating forms of cancer and inflammatory disease. One antisense drug for the treatment of cytomegalovirus is in the market today.

Monoclonal antibodies were trumpeted as new "miracle" drugs when the method to produce them first appeared nearly 30 years ago. They are just now appearing in the pharmaceutical market. Antisense has not been a "bust." Rather, the development of antisense methods is following a characteristically difficult, expensive, and highly regulated path from laboratory to clinic.

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Lateral Gene Transfer or Viral Colonization?

S. L. SALZBERG AND COLLEAGUES REEXAMINED data that had been published by the international human genome sequencing group in which it appeared that between 113 and 223 genes were present in the human genome but were absent from lower eukaryotes (*Caenorhabditis elegans, Saccharomyces cerevisiae, Drosophila melanogaster, Arabidopsis thaliana*) (Reports, "Microbial genes in the human genome: Lateral transfer or gene loss?", 8 Jun., p. 1903). This result had suggested that these genes had undergone direct bacterial-to-vertebrate transmission (lateral transfer). From their reevaluation of this set of genes and inclusion of genomes of additional eukaryotic parasites, Salzberg and colleagues conclude that many of these candidate transfer genes appear to have been lost from the original lower eukaryotic set and that gene loss is the more plausible explanation for this result. In an accompanying Perspective ("Are there bugs in our genome?", p. 1848), Jan O. Andersson and co-authors note that at least some of these genes (the *N*-acetylneuraminate lyase, for example) retain a phylogenetic pattern consistent with lateral transfer.

Neither of these papers, however, considers an alternative possibility that we had published (*1*), namely, that viral colonization of host genomes can account for apparent lateral transfer between distantly related organisms. This idea suggests that viruses can originate genes, then colonize either prokaryotes or eukaryotes to give the appearance of lateral gene transfer.

In prokaryotes, it is becoming increasingly clear that most genomic differences between groups are due to infectious events involving acquisition of new gene sets. We reported that the eukaryotic replication proteins appear to have been obtained from viral, not prokaryotic, sources because phycodnaviral DNA polymerase was phylogenetically ancestral to the replicative polymerase of eukaryotes. Because viruses (especially large DNA viruses) can persistently infect host prokaryotic and lower eukaryotic genomes and because they have an enormous capacity for creation of genetic novelty through recombination, viruses can explore more sequence space and at a more rapid rate than their cellular hosts. In figure 2 of their report, Salzberg *et al.* examine hyaluronan synthase as a possible example of lateral gene transfer. Although bootstrap values are not presented, the resulting phylogeny shows that the gene from phycodnavirus is basal to those found in vertebrates (but is still absent from lower eukaryotes). We suggest that this can support the idea that this gene originally colonized vertebrates from a virus.

"This idea suggests that viruses can originate genes, then colonize either prokaryotes or eukaryotes to give the appearance of lateral gene transfer."

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1. L. P. Villarreal, V. R. DeFilippis, *J. Virol.* **74**, 7079 (2000).

Response

DEFILIPPIS AND VILLARREAL RAISE AN EXCELLENT point: Integration of viral DNA into the genomes of free-living organisms might explain the presence of atypical genes in many species. If related viral genes independently made their way into different genomes, this could lead to mistaken conclusions about lateral gene transfer. To explore this possibility, we searched all of the genes considered as possible bacteria-to-vertebrate lateral transfers (BVTs) against all viral genes from the public databases. No significant matches between BVTs and viral genes were found, and therefore we did not have anything to report in our original study. We did find significant viral matches for some of the possible BVTs proposed in (*1*). Of the many phylogenetic trees that provided evidence against lateral gene transfer, the one that we chose to show in our figure 2 was selected because of the presence of a viral homolog. To determine whether the hypothesis of DeFilippis and Villarreal is correct, many more viral genomes need to be sequenced.

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References and Notes
1. International Human Genome Sequencing Consortium, *Nature* **409**, 860 (2001).

CORRECTIONS AND CLARIFICATION

REPORTS: "Haplotype variation and linkage disequilibrium in 313 human genes" by J. C. Stephens *et al.* (20 Jul., p 489). The SNPs identified and characterized for this report were deposited in the Database for Single Nucleotide Polymorphisms (dbSNP) under identification numbers ss3178318 through ss3182216, without interruption. The correspondence of these numbers to each SNP is also provided at http://www.genaissance.com/genecharacteristics/genecharacteristics.pdf. Information about individual SNPs can be viewed by submitting the ss numbers to the dbSNP search tool at http://www.ncbi.nlm.nih.gov/SNP/index.html

RESEARCH ARTICLES: "Evidence for substantial variations of atmospheric hydroxyl radicals in the past two decades" by R. G. Prinn *et al.* (8 Jun., p. 1882). On page 1883, three formulae were incorrectly printed. Equation 3 should have appeared as $\mathbf{P}(+) = (\mathbf{1} - \mathbf{KH})\mathbf{P}(-)$, with "1" in bold face instead of roman type. Equation 4 should have appeared as $\mathbf{K} = \mathbf{P}(-)\mathbf{H}^{\mathrm{T}}[\mathbf{HP}(-)\mathbf{H}^{\mathrm{T}} + \mathbf{R}]^{-1}$, with the bracketed expression raised to the power "–1." And in paragraph 2, column 3, the equation for f should have appeared as $f = a + bP_1(t) + (c/3)P_2(t)$, with the coefficient c divided by 3.

LETTERS: "Portugal: A case history in S&T cooperation" by E. McSweegan (30 Mar., p. 2549). Note 1 for the Luso-American Development Foundation should have read simply http://www.flad.pt.