

proposal would, very likely, have been declined—not because of poor quality but because of lack of perceived relevance of separate parts of the research to the mission of the different agencies.

While we do not advocate duplicate proposals, my division encourages joint agency submission when this would promote closer cooperation between agencies. This, we feel, is important to the special character of our research community and is helpful in fostering interdisciplinary research teams and cultivating interdisciplinary research efforts.

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Combating Epidemic Cholera

R. I. Glass *et al.* (Perspectives, 12 June, p. 1524) exaggerate the protective efficacy of killed whole-cell oral cholera vaccines that were evaluated in Bangladesh for 3 years (1). The data from (1) indicate that the protective efficacy in the third year, in terms of cholera episodes in recipients of three doses of the oral whole-cell vaccine, was 43% (not "more than 70%") and, paradoxically, addition of the

cholera toxin B subunit to the vaccine reduced that figure to 17%. Although higher protective efficacies were attained in adults during the first 2 years after the three-dose regimen, the vaccines were practically ineffective in children, the targeted population in heavily endemic areas like Bangladesh. The vaccines were also somewhat more effective against classical biotype cholera than against the El Tor biotype, which is currently sweeping through the Western Hemisphere.

As these dead oral vaccines are expensive, difficult to administer, insufficiently protective, and potentially nonreproducible (they were constructed arbitrarily and there are no bioassays that reliably predict efficacy), the reader should not come away with the impression that they offer a solution to the cholera problem in the Americas or elsewhere. As Glass *et al.* stated, oral rehydration therapy is effective and relatively cheap. Intelligent epidemiological control measures can help, but the best solution resides in providing safe drinking water and sewage disposal. This can be an expensive investment, but it is one that will also reduce the burden of other diarrheal diseases, which, in some heavily afflicted areas, kill half the children before they reach the age of five.

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References

1. J.D. Clemens *et al.*, *Lancet* **335**, 270 (1990).

Nucleoside Diphosphate Kinase: Conclusions Withdrawn

We wish to call the readers' attention to technical errors in our report "Activation of a small GTP-binding protein by nucleoside diphosphate kinase" (8 Nov. 1991, p. 850) (1). As a result of these errors, our principal conclusions must be re-evaluated. We reported activation of the adenosine diphosphate ribosylation factor (ARF) by an *in situ* phosphorylation of bound guanosine diphosphate (GDP) by nucleoside diphosphate kinase (NDK). In the course of extending the results of this paper, we have discovered several artifacts of the techniques we used in our tests of our hypothesis. We have now documented each of the problems and have expanded our studies to include p21 *ras* and transducin (2).

First, NDK activity survives the polyethylimine (PEI) thin-layer chromatography procedure used to analyze products of the reaction, while guanosine triphosphate (GTP) binding proteins do not. Second, GDP binding is stabilized by high concentrations of protein (including NDK). The combination of these two artifacts led to the following circumstances. At low NDK concentrations GDP dissociation was underreported, and phosphorylation of free GDP was responsible for all product formation. At high NDK concentrations NDK activity surviving on the PEI plates was sufficient to phosphorylate all of the GDP released from the PEI-denatured GTP-binding protein.

We would like to emphasize that the results in our *Science* paper are artifactual and that these artifacts appear to pertain to several GTP-binding proteins in addition to ARF. The observations are reproducible, but misleading. Therefore, we apologize for any confusion or wasted effort our report might have caused.

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1. P. A. Randazzo, J. K. Northup, R. A. Kahn, *Science* **254**, 850 (1991).
2. P. A. Randazzo *et al.*, *J. Biol. Chem.*, in press.

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