Response: The model that we used in our report (1) is not incorrect. We would have arrived at the same conclusion regarding the seawater Sr isotopic consequences of Larson’s crustal production rates during the mid-Cretaceous (2) had we considered in our report only the extrusive part of oceanic crustal production. This consideration would involve two changes to the model. The first would be to convert the total crustal production rate provided by Larson to the extrusive component by dividing the values by five (because, as Larson points out, the ratio of extrusive to intrusive is relatively constant at about 1 to 4, or 1 to 5). The second change would be to calculate the Sr exchanged per cubic kilometer of extrusive rocks. Given that the total amount of Sr exchanged is fixed at 1.2 × 10^10 mol per year (for 20 km^3 of total crust or 4 km^3 of extrusive component), the exchange per cubic kilometer of extrusives will be five times greater than that calculated for the oceanic crust as a whole. The combined effect of considering changes in the production rate of extrusives and attributing all Sr exchange to the extrusive part of the oceanic crust results in exactly the same calculated change in the Sr isotopic composition of seawater for the oceanic crustal production rates given by Larson (2). Thus it appears that the “incorrect use of crustal volume data” noted by Larson is irrelevant.

Larson suggests that a 28% increase in crustal production rates (not accounting for plateaus) during the mid-Cretaceous “is a close match to the largest increase calculated by Ingram et al. in hydrothermal flux.” However, the value that we calculated based on our Sr data is 15% (1); not the 25% estimated by Larson from our figure 2. Following the equation given in our paper (1, p. 549), one can calculate that a 28% change in the hydrothermal flux would produce a change of 40 Δ^87Sr units while the actual data show a change of only half that amount. Furthermore, the 28% change in crustal production rate mentioned by Larson is an average for a period lasting some 40 million years, while the seawater Sr isotopic data indicate a period of low Δ^87Sr lasting no more than 10 million years.

As summarized in our report (1), the mid-Cretaceous is an exceptional time in terms of oceanic volcanism, high sea level, high global temperature, and the preservation of large amounts of organic carbon, and yet the Sr isotopic composition of seawater, which is often assumed to be a useful monitor of global processes, shows little change. Further, we addressed the question of how much change in the Sr isotopic composition of seawater would result from the much larger oceanic crustal production rates suggested by Larson (2) under the assumption that new oceanic crust in the Cretaceous exchanges Sr in much the same way as does presently forming oceanic crust. All other factors in the Sr budget of seawater were for the purposes of this intellectual exercise held fixed. The result was that we calculated a decrease in Δ^87Sr of seawater that is five times larger in amplitude and five times longer in duration than what is observed. The only discernable effect was a decrease in Δ^87Sr coincident with and proportional to the emplacement of the large oceanic plateaus. Perhaps changes in the hydrothermal Sr exchange from increased ocean crust production were compensated by almost exactly the right changes in the riverine flux of Sr. We noted that possibility in our report (1), but still believe it to be unlikely. Perhaps, as Larson points out, it is a result of mid-Cretaceous oceanic volcanism having different Sr exchange properties than present-day oceanic volcanism. If that is the case, one should be especially cautious in using the high rate of oceanic volcanism during the mid-Cretaceous to explain other aspects of ocean chemistry during that period. Alternatively, perhaps the mid-Cretaceous ocean production rates are not entirely correct. Larson himself (2, p. 548) states “there are large assumptions in the calculation of Pacific ridge volume that probably never can be verified, but they must be utilized if such a worldwide calculation [of ridge production] is made.” Thus it seems appropriate to use the Sr isotopic composition of seawater during the mid-Cretaceous to verify (or deny) some of these “large assumptions.”

Larson mentions a paper by Jones et al. (3) that appeared after our report. Rather than respond to Larson’s assertion that the paper by Jones et al. (3) produced a more “quantified and successful” model than ours, we suggest that interested persons read both and reach their own conclusions.

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REFERENCES

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Mutant Mice, Cu,Zn Superoxide Dismutase, and Motor Neuron Degeneration

In their report of 17 June, Mark E. Gurney et al. (1) describe a transgenic mouse model for amyotrophic lateral sclerosis (ALS) that overexpresses a mutant human gene encoding Cu,Zn superoxide dismutase (SOD) and that also normally expresses mouse SOD, resulting in a fourfold increase in total SOD activity. A large literature shows that overexpression of SOD causes a paradoxical oxidative stress not unlike that associated with the underexpression of the gene. Gurney et al. do not cite this literature, however, and instead interpret their result to mean that familial ALS is not a result of the fact that these individuals have about 50% less SOD activity in their cells, but rather of some new but unknown activity (a gain-of-function) coincidently shared by the dozen or so mutant forms of the human SOD found so far in ALS patients.

Elroy-Stein et al. (2) noted substantially increased lipid peroxidation in transfected cells overproducing native human SOD by a factor of 3.6 and estimated that overexpression of SOD beyond a factor of 6 is probably lethal. Norris and Hornsby similarly concluded that overexpression of SOD is lethal to transfected adrenocortical cells (3).

We have reported that for any given rate of superoxide production there exists a concentration of SOD that will produce a minimum amount of oxidative stress and lipid peroxidation. This is a result of the paradoxical abilities of the superoxide radical to both initiate and terminate lipid peroxidation (4). Initiation is indirect, by the liberation and reduction of iron.) Thus, when exogenous SOD is used to restore oxidative balance to a tissue in oxidative stress, such as a postischemic isolated heart, it exhibits a relatively sharp bell-shaped dose-response curve (5). A unique concentration of the enzyme provides maximal protection; either more or less than this concentration leads to increased lipid peroxidation, increased biochemical markers of tissue damage, and loss of function. The transgenic “ALS mouse” expresses four times more SOD activity than a normal mouse. The oxidative stress and increased lipid peroxidation resulting from this degree of overexpression would be substantially greater than that produced by ex-
Response
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