Reply to Kelly et al.

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REPLY: We thank Kelly and coworkers (3) for their comments. We agree that some of the Ren-2 animals in our study did develop malignant hypertension, as discussed in our report (see the penultimate paragraph of the DISCUSSION in Ref. 1). We included all animals which survived to the end of the study in the final analysis because we feel that the exclusion of animals with malignant hypertension would have confounded the results. First, exclusion before entry in the protocol is not possible because Ren-2 rats can develop malignant hypertension over several months (5). Second, early signs of malignant hypertension such as increased diuresis or weight loss are of little use in diabetic animals and could be used only in normoglycemic controls. A marked weight difference between diabetic and nondiabetic Ren-2 rats is obvious in our study as well as in the reports of Kelly and coworkers (2, 4). Third, exclusion of animals with malignant hypertension based on criteria like blood pressure or renal damage could obviously lead to a bias, especially if malignant hypertension occurs more frequently in one group.

We observed some diabetes-induced glomerular matrix expansion superimposed on hypertension but no nodular glomerulosclerosis. The lower mortality in diabetic Ren-2 rats (Fig. 6C in Ref. 1) certainly does not point to more severe kidney damage either. Finally, we are surprised to read in the letter by Kelly and coworkers that they were “always careful to exclude” animals with malignant hypertension. No such statement can be found in their reports (2, 4). A procedure that bears such a high potential to affect the results should not be omitted from the description but needs to be clearly outlined.

REFERENCES