the clinical significance of this change at this time remains unknown.

Drs Shamseddin and Gupta suggest that further studies are required before we 'substitute MMF/CNI with the MMF/SRL regimen'. We would agree that no immunosuppressive regimen is right for everyone. We believe that, given the similarity of results from the STN experience in the United States and the results of the CONCEPT[3] study conducted in France, these two regimens, for at least the first 2 years post-transplant, were therapeutically equivalent, albeit with a different side effect profile. What will be important is longitudinal follow-up of these two studies in order to validate the durability of these 2-year observations. As with any form of chronic immunosuppression, there is a learning curve that takes many years. Fortunately, given the results of studies such as CONCEPT and STN, we have a better picture as to how best to incorporate the use of mammalian target of rapamycin inhibitors during the first 2 years post-transplantation. We thank Drs Shamseddin and Gupta for their critical comments.

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Matthew R. Weir[1]
[1]*Division of Nephrology, University of Maryland School of Medicine, Baltimore, Maryland, USA*
Correspondence: *Matthew R. Weir, Division of Nephrology, University of Maryland School of Medicine, N3W143 Nephrology, UMMS, Baltimore, Maryland 21201, USA. E-mail: mweir@medicine.umaryland.edu*

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Does renalase degrade catecholamines?

To the Editor: Wu *et al.*[1] recently reported that renalase deficiency alone is associated with hypertension and susceptibility to ischemic myocardial damage. They contend that renalase's cardioprotective effects are mediated by its ability to metabolize catecholamines. The hypothesis that renalase could degrade catecholamines was first proposed given its moderate sequence homology to monoamine oxidases.[2] However, it is our opinion that no concrete evidence exists in the literature to directly support this hypothesis. Wu *et al.*[1] refer to the publication[2] that first observed potential catecholamine-degrading activity for renalase. However, the methodology employed to arrive at this observation has been questioned.[3] Furthermore, the rate of catecholamine degradation was thought to be too low to be ascribed to enzymatic activity.[3] Recently, Pandini *et al.*[4] showed that structurally sound recombinant renalase did not metabolize catecholamines.

The renalase-deficient mice studied by Wu *et al.*[1] were generated from C5BL/6 mice. Nucleotide sequences encoding renalase in wild type (C57BL/6) published at Ensembl and NCBI do not encode proteins with flavin adenosine dinucleotide or nicotinamide adenine dinucleotide-binding sites. Our own sequencing of renalase transcripts from various mouse strains demonstrates that renalase in these animals is shorter than rat and human renalase and does not contain the N-terminal flavin adenosine dinucleotide-binding site characterized by a GxGxxG motif, as described by Wu *et al.*[1] It would have been informative for the authors to provide a sequence alignment of C5BL/6 renalase and human renalase to illustrate this point. It is difficult to comprehend how renalase normally functions in mice if the protein does not possess this supposedly essential active site.

Although renalase may well have an important physiological role in the context of hypertension and cardio-renal disease, this appears unlikely to be mediated by degradation of catecholamines.

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Nina Eikelis[1], Sarah C. Hennebry[1], Gavin W. Lambert[1] and Markus P. Schlaich[1]
[1]*Neurovascular Hypertension and Kidney Disease, Baker IDI Heart and Diabetes Research Institute, Melbourne, Victoria, Australia*
Correspondence: *Nina Eikelis, Neurovascular Hypertension and Kidney Disease, Baker IDI Heart and Diabetes Research Institute, PO Box 6492, St Kilda Road Central, Melbourne, Victoria 3008, Australia. E-mail: nina.eikelis@bakeridi.edu.au*

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The Author Replies: Eikelis *et al.*[1] suggest that the cardiac and hypertensive phenotype of the renalase knockout (KO) mouse[2] is unlikely to be mediated by renalase's ability to metabolize catecholamines, and also question the notion that renalase metabolizes catecholamines.

The renalase KO was maintained on a mixed background (129Sv/J and C5BL/6) as detailed in the Materials and Methods section. Sequence analysis of 129Sv/J genomic DNA revealed the presence of the N-terminal flavin adenine dinucleotide-binding site of renalase. Additionally, complementary DNA sequence from NOD (EMBL-Bank: AK170321.1) and Kunming (EMBL-Bank: DQ788834.1) mouse strains confirm the presence of the flavin adenine