Author’s response to reviews

Title: Cortical and trabecular bone are equally affected in rats with renal failure and secondary hyperparathyroidism

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Author’s response to reviews:

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Dr. Hayley Henderson
Editor
BMC Nephrology

Re: Submission of revised manuscript (BNEP-D-17-00299-R1)

Dear Dr. Henderson:

Thank you for your email dated November 20, 2017 and the reviewer comments for our revised manuscript entitled, “Cortical and trabecular bone are equally affected in rats with renal failure and secondary hyperparathyroidism”.

We have further addressed the minor comments made by the reviewers and made appropriate changes. We hope that the revised manuscript is now acceptable for publication in BMC Nephrology.

Please let me know if you need any further information.

Thank you for consideration of our paper.

With best wishes and regards,
Once again, we thank the reviewers and the editor for their comments. We have now further amended the paper by responding to the review comments as stated below.

Ferruh Artunc (Reviewer 1): The authors have adequately revised their manuscript. However, the point with the high phosphorus diet in a renal failure model remains counterintuitive. It would be better to rephrase it with hyperphosphatemia as mentioned in the rebuttal letter. The authors should allude to the expected effects of low phosphate diet to reduce SHTP and cite the paper of Bohnert BN et al. (Impact of phosphorus restriction and vitamin D-substitution on secondary hyperparathyroidism in a proteinuric mouse model. Kidney Blood Press Res., 2015).

Response: Discussion section, lines 269-279, page 11: We have now rephrased the statement in the manuscript as recommended by the reviewer and also included the reference of Bohnert et al.

Pascal Houillier (Reviewer 2): Concerns 1 and 2. At least, the authors could have addressed the limits of their model in the discussion.

Response: Discussion section, lines 269-285, page 11: We have now addressed the limitations of the model used in the discussion.

Concern 3. There is some misunderstanding here. Actually, creatinine can be used to show that GFR is decreased, compared with a control group, or even to follow the course of GFR over time. However, at D19, creatinine level in Nx rats is more than twice as high as in control rats. This reviewer is unsure this corresponds to "early" CKD, unless measured GFR shows that the decrease is mild, as compared with the control group.

Response: Discussion section, lines 259-260, page 10: The changes in creatinine levels observed in our study are consistent with what others have reported in other rat models of CKD. We have referenced these papers in the discussion.

Concern 4. The authors have added the R2 and p values. Still the plots on Fig.7 are highly scattered and not quite convincing. In addition, as already mentioned, no attempt to get any insight into the molecular mechanisms going on has been made.
Response: Discussion section, lines 279-283, page 11: The highly scattered plots could be due to a number of reasons including: a) small number of replicates per group used in the study; b) biological variation in disease status in different animals; and c) dilution of the relative contribution of measured parameter to CKD due to involvement of multiple signaling pathways. We have added this in the discussion.

Discussion section, lines 218-267, page 9-11: We have briefly elaborated on the potential mechanisms for reduced bone mass during kidney failure in the discussion. However, further studies are needed to evaluate the potential cause and effect relationship between changes in calcium regulating hormones and growth factors to reduced trabecular bone mass in response to partial nephrectomy.