**Author's response to reviews**

**Title:** Effects of Lovastatin Treatment on the Metabolic Distributions in the Han:SPRD Rat Model of Polycystic Kidney Disease

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RE: Submission of the revised manuscript MS: 1052217702976680 entitled: “Effects of Lovastatin Treatment on the Metabolic Distributions in the Han:SPRD Rat Model of Polycystic Kidney Disease”

Please find attached the revised manuscript titled above, which we would like to resubmit for a publication in BMC Nephrology.

Our study showed that PKD animals show increased levels of inflammatory bioactive lipid markers derived from the metabolism of arachidonic acid by 5-LOX and 12/15-LOX enzymes. In addition, levels of the endothelial dysfunction marker SAH are increased as well in plasma of PKD animals, and PKD kidneys show a decreased Krebs cycle activity and an increased production of uric acid oxidation product allantoin. Lovastatin decreased measured inflammatory markers, specifically the above mentioned 13-HODE, 12-HETE and leukotriene B4. In addition, lovastatin was successful in reducing the elevated homocysteine and allantoin levels and it also increased plasma arginine, thus positively affecting the NO production and vascular function in cystic animals. In terms of cell metabolism, treatment with lovastatin increased citrate as well as the glycolytical lactate production, thus improving the overall energy state of the cystic kidney. Taken together, our results describe the potential mechanisms of how lovastatin reduces PKD and support the clinical studies of statins that are underway in patients with ADPKD. In addition, the identified pathways could be used as potential therapeutic targets for slowing down the cyst growth.

Thanks you very much for the consideration.

Cordially,

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