Author’s response to reviews

Title: Pirfenidone prevents Acute Kidney Injury in the Rat

Authors:

Francesco Fontana (francescolorenzofontana@gmail.com)
Ixchel Lima Posada (ixchel_1023@hotmail.com)
Rosalba Pérez Villalva (melibiosa@hotmail.com)
Nathan Berman Parks (superberman@gmail.com)
Norma A Bobadilla (nab@biomedicas.unam.mx)

Version: 4 Date: 08 Feb 2019

Author’s response to reviews:

México City February 08th, 2019.

Dr. Hayley Henderson,
Editor-in-Chief

Dear Dr. Henderson:

We are re-submitting the following manuscript for consideration in the BMC Nephrology: “Pirfenidone prevents Acute Kidney Injury in the Rat”

We thank to the reviewers for their positive observations and comments. As a result, we modified all the graphs, as was suggested by the reviewer and now they appear as mean ± standard deviation, instead of standard error.

We appreciate the opportunity to publish our manuscript in BMC Nephrology
Sincerely,

Norma A. Bobadilla PhD.
Senior Researcher
Instituto de Investigaciones Biomédicas,
Universidad Nacional Autónoma de México and
Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán
e-mail: nab@biomedicas.unam.mx or norma.bobadillas@incmnsz.mx

Reviewer 1

Mark De Caestecker (Reviewer 1): I accept your argument about statistical power. Please include this in statistical methods based on your own lab data. In addition, please graph actual values (dot plots with mean and SD) for BUN, creatinine clearance and RBF, so that the readers can see the actual variance in these key functional data.

FYI: to the argument that this is the standard in the literature (4-6 rats per group), I think this is a false argument. Much of the literature is littered with falsely positive, underpowered pre-clinical studies that are published because of the selection bias for positive data. My own personal experience with functional assessments and power analysis based on our own data and direct of GFR in mice (granted not rats), tells me that 4-6 animals per group is inadequate, and the only thing worse from the 3R perspective, is performance of underpowered studies, where the findings have an increased likelyhood of being false given the publication environment we currently have.

We modified all the graphs, as was suggested by the reviewer, and now they appear as mean ± standard deviation, instead of standard error. In addition, we added the p value of RBF, BUN and GFR in the results section and these parameters are presented as dot plots in Figure 1.
In relation to the number of animals used, we agree with the reviewer that in mice it is necessary to include at least 8 animals, because the mice exhibit great variability. However, this is not the case in the rats, in which the variability is much lesser. We have extensive experience in this model of ischemic injury in the rats and any maneuver that improve renal function is also corroborated at histological level that is the gold standard to evaluate the tubular injury induced by ischemia/reperfusion. I hope this argument will be more convincing based in our experience.