Reviewer’s report

Title: Pirfenidone prevents Acute Kidney Injury in the Rat

Version: 1 Date: 18 Sep 2018

Reviewer: Mark De Caestecker

Reviewer's report:

This paper describes the effects of pretreating rats undergoing bilateral IR-AKI with the anti-fibrotic and anti-oxidant Pirfenidone. Data show a clear effect on PF on reducing short-term injury (histology) and renal function (creatinine clearance and urine output) 24 hours after injury, associated with reduced urinary HSP72 (a tubular injury biomarker recently described by this group), as well as increased urinary nitrates and nitrites. Over all the data are convincing but I am concerned that will the small numbers of rats studied (only 6 in each group) this may represent a chance finding.

Major criticisms

1) Low rat numbers to assess functional recovery from IR-AKI

Minor criticisms

1) Marked tissue injury despite short clamp times (20 minutes) needs to be discussed in relation to other data from the same lab

2) Background discussion about the central role of NaK ATPase on epithelial polarity is debatable and unnecessary for the background

3) Methods should specify the strain of rats used

4) IR-AKI controls need to be vehicle treated and information about the volume and vehicle used for PF treatment needs to be described

5) Rats are placed in metabolic cages 2 hours after surgery. I assume rats have been habituated to the metabolic cages beforehand. If so, please state this. If not, provide a rationale why this was not done

6) Provide references for the use of urinary HSP72 as an AKI biomarker: it is not commonly used
7) Provide figure legends to illustrate graph bars

8) The statement that eNOS mRNA was reduced by T-Test but not ANOVA, is meaningless and should be removed. You can state that eNOS levels increased with PF treatment but this did not reach the level of statistical significance. That said, this could easily be a false negative result because of the small numbers of animals used

9) Provide scale bars in the microscopy images

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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