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SUPPLEMENTUM 2023

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Title:

Hypoxia-inducible factors activator, roxadustat, increases pulmonary vascular resistance in rats

Author(s):

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Reviewer's comments to authors:

The study by Novak et al. describes the acute and chronic effects of stabilization of HIF transcription factors by a prolyl hydroxylases inhibitor (roxadustat) on the pressure-flow relationship of isolated perfused rat lungs and on the vasoconstrictor effects of angiotensin II and chronic hypoxia with regard to the possible role of ACE2. The results showed that roxadustat increased the risk of pulmonary hypertension but did not affect pulmonary vascular reactivity. ACE2 activator led to pulmonary vasoconstriction. The experiments were carefully conducted and the results are interesting.

The rationale for examining the effects of ACE2 activator on pulmonary vascular reactivity is not clear from the abstract and should also be better explained in the introduction (i.e., with respect to the action of roxadustat and the effect of ACE2 on pulmonary hypertension).

It is commendable that the authors also report unexpected paradoxical results regarding the constrictive effect of ACE2 activator on the pulmonary vasculature. However, the absence of any attempt at a possible explanation can be considered a limitation of the study.

A diagram of experiments on isolated perfused lungs would be helpful.

Data in the text describing basal perfusion pressure and the intercept of P/Q lines with the pressure axis could be added to the table for clarity.

The table and figure should show the number of animals for each group. The group labelled Rox2w in the figure and table is labelled R2w in the text.

Reviewer´s opinion:

Does the work presented in the paper contain enough new material to warrant publication?

yes no

Is the article of high scientific quality?

yes no

Are the literature citations appropriate and adequate?

yes mistakes no

Are the descriptions of tables of data, figures etc. relevant and sufficient for understanding of the presented work?

yes partially no

Paper acceptance

- without changes
- after minor revision
- after major revision
- to be rejected

Priority

- high
- medium
- low

Referee wants to see yes

no

the manuscript
after revision

Reviewer´s comments to editors (confidential):

Jedná se o dobře provedenou práci zkušeného týmu, která by po úpravě měla být akceptovatelná.