Reviewer 2 v. 1

Comments to the Author

The aim of the study by Hodge et al. was to demonstrate decreased levels of SIRT1 in

CD28nullCD8+ T and NKT-like lymphocyte subsets in patients with COPD, and that treatment with prednisolone, in combination with theophylline, curcumin and/or resveratrol could increase SIRT1 expression, restore steroid sensitivity and inhibit pro-inflammatory cytokine production thus reducing systemic inflammation in COPD.

Although the subject is very interesting and the manuscript overall well written, some explanations are required.

o First of all, authors talk about “steroid-resistant senescent cells” but the underlying

mechanism is unclear. Probably because these cells express reduced levels of GCR? Please, explain better this key concept.

o In the abstract, western blot is used to determinate “expression of CD28, SIRT1 and pro-inflammatory cytokines”, but the protocol is not described in the Material and Methods section. What was exactly measured with the western blot?

o In the line 319 is written “….GCR expression in CD28null and CD28+ CD8+ T cells from a COPD patient…”, why from only one patient?

o Why results with EX-527, SRT720 on SIRT1 and intracellular cytokine expression are not showed? Where are results on effect of therapies on GCR expression, as mentioned in the specific paragraph in the material and methods section?

Furthermore, images and figures are of bad quality and should be revised. They are too small and not sharp. Then, there are some typing errors or punctuation inaccuracies. Please, read again the manuscript.

Finally, please revise bibliography about SIRT1 levels in peripheral blood lymphocytes, adding other references (e.g: Oxid Med Cell Longev. 2018;2018:9391261.; Am J Respir Cell Mol Biol. 2015;53(6):782-92….)