Reviewer 1 v.1

Comments to the Author

In this manuscript the authors have demonstrated decreased SIRT1 expression in peripheral CD8 lymphocytes and correlated this to increased inflammation and features of COPD. The manuscript is an incremental in that the role of SIRT1 as an anti-aging and anti-senescence is well known. It is also well known that senescence leads to secretion of pro-inflammatory cytokines. Also well known that SIRT1 activators can rescue aging and senescence. The authors just take this a step further to demonstrate this in another cell type.

The authors miss an important opportunity to link SIRT1 suppression to other downstream stages like impaired mitophagy and senescence which is something that can be easily done using stains. A lot of data mentioned in the manuscript text can be graphed or tabulated to improve the manuscript. For instance, “Increased CD28null CD8+ T and NKT-like cells in COPD” would be better tabulated perhaps as Figure 1A. Likewise, TNF-α production by COPD group should be shown.

While the authors mention that SIRT1 and GCR colocalize in Hela cells, they only shown co-expression in their lymphocyte subset. A simple two color staining would show colocalization in lymphocytes as well. Moreover, co-expression is not very surprising given that SIRT1 is a housekeeping gene and is expressed by most cell types. This data really proves nothing.

Figure 8A and B should be plotted as % levels to better understand the outcomes instead of % increase or % decrease.

On the whole the manuscript provides incremental information for another cell type. Including data that can provide some mechanistic information will significantly improve the manuscript.