

### **Responses to the comments by Reviewer 02363472**

We appreciate kind reviewing of our manuscript. In our revised manuscript, we described detail information regarding the names of drugs that were used in the article by Jones et al. We also added several descriptions about the possible mechanisms of the development of anti-HIV agent-based lipodystrophy (page 4, lines 12-16).

### **Responses to the comments by Reviewer 02955164**

We truly appreciate kind and very careful reviewing of our manuscript.

[Point-by-point responses]

- 1) We have provided the complete reference of the article by Jones et al. in the abstract.
- 2) We have properly paginated the manuscript.
- 3) We have corrected and retyped the word “LIPODYSTROPHY” in the subheading in page 2.
- 4) We have moved “[2]” to the right position.
- 5) We have corrected "Jones E et al" as "Jones et al" in Figure 1.
- 6) We have added the following sentences by referring the two important papers that the reviewer kindly showed (page 4, lines 12-16).

“In addition to suppressing growth and differentiation of preadipocytes<sup>[1]</sup>, protease inhibitors reportedly exert multifactorial effects on adipocytes including impairment of mitochondrial functions<sup>[14]</sup>, changes in the gene expression related to ER-stress and lipid droplet formation<sup>[14]</sup> and even an induction of mitophagy<sup>[15]</sup>.

[Added references]

14. **Bociąga-Jasik M**, Polus A, Góralaska J, Czech U, Gruca A, Śliwa A, Garlicki A, Mach T, Dembińska-Kieć A. Metabolic effects of the HIV protease inhibitor--saquinavir in differentiating human preadipocytes. *Pharmacol Rep.* 2013; **65**: 937-950. PMID: 24145088
15. **Gibellini L**, De Biasi S, Pinti M, Nasi M, Riccio M, Carnevale G, Cavallini GM, Sala de Oyanguren FJ, O'Connor JE, Mussini C, De Pol A, Cossarizza A. The protease inhibitor atazanavir triggers autophagy and mitophagy in human preadipocytes. *AIDS.* 2012; **26**: 2017-2026. PMID: 22948272 DOI: 10.1097/QAD.0b013e328359b8be

**Responses to the comments by Reviewer 00504167**

We truly appreciate kind reviewing of our manuscript.

**Responses to the comments by Reviewer 00484099**

We appreciate kind reviewing of our manuscript. According to the comment by the reviewer, we have revised the figure 1 and its legend.