Reviewer’s report

Title: Ethanol extract of propolis protects macrophages from oxidized low density lipoprotein-induced apoptosis by inhibiting endoplasmic reticulum stress-C/EBP homologous protein pathway

Version: 3 Date: 26 April 2015

Reviewer: tomomi Prof. gotoh

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Comments to Tian et al. paper,

(General comments)

In this paper, Tian et al. showed that treatment with Ethanol extract of propolis (EEP) suppress ox-LDL-induced apoptosis as ER stress-inhibitor PBA in macrophages. They also showed that EEP treatment suppress induction of ER stress-CHOP pathway through suppression of ox-LDL intake and the up-regulation of CD36 induced by ox-LDL in macrophages.

The data shown here are clear and meaningful. However, there are some questions concerning their conclusions. In Fig. 2&5, the authors show EEP suppress TM-induced ER stress pathway. If EEP suppress ox-LDL-induced apoptosis through suppression of ox-LDL intake and the up-regulation of CD36 induced by ox-LDL, the mechanisms how EEP suppresses TM-induced ER stress pathway remains unknown. The authors should elucidate those mechanisms.

(Specific comments)

1. In Fig2C, the author should show the LDH activity in the case of total cell death as the positive control.

2. If the mechanisms of the suppression of ER stress pathway are different between EEP and PBA, treatment with both EEP and PBA show synergetic effect?

3. In Fig. 4A, GRP78 show double bands, but, in Fig. 5A, GRP78 show single band. The authors should mention about this point.

4. In Fig. 4A, induction of CHOP is barely suppressed by the treatment with PBA. However, in this condition, apoptosis is effectively suppressed in Fig. 3A. The authors should mention about this point.

5. In Fig. 4A&5A, the authors should show also the results of total PERK and eIF2a.

6. To show the mechanisms of the suppression of ER stress pathway, the authors should show the results of other ER stress-specific molecules such as IRE1, ATF6, XBP1.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

Nothing to declare.