In the manuscript, the authors induced diabetes in 120 mice, other 40 served as non-diabetic controls. One hundred twenty mice were divided into large three groups (40 mice each): the first and the second group were treated with b2GPI and reduced b2GPI, respectively. The third group was served as diabetic control. The first and the second group were divided into two different protocols in terms of b2GPI injection (single and twice). The authors measured lipid profiles, atherosclerosis of the aorta, metalloproteinase expression and MAPK activity in the aortic endothelial cells.

The authors conclude that reduced b2GPI down-regulate p38MAPK, decreases MMP expression and work protective for athelosclerosis.

1) Major Compulsory Revisions
This reviewer does not understand why one treatment group comprise 20 mice and non-diabetic control as well as diabetic control require 40 mice. Is this really approved by ethics committee?

Throughout the manuscript, English literature requires intensive proofreading. Sometimes it is very difficult to understand what the authors try to explain.

Many of the figures are unclear. In particular, panels indicating the results of immunoblot are sometimes too small to include the indicated bands. Error bars in each figure needs to be explained in the legends.

Only comparisons between two groups are shown in the results as well as figures. Results of the statistical analyses among four groups need to be provided.

In figure 1, single dose of b2GPI decreased LDL-c, but complex dose did not. This cannot be explained.

In figure 2, difference in the atherosclerotic area of diabetic control mice between “mono dose” and “complex dose” is unacceptably different, although these two results should be similar.

The result of Figure 3 needs to be quantified.

The result indicated in Figure 4 and 5 is interesting because reduced b2GPI suppress the expressions of MMP2 and MMP9. Was this experiment really done in 20 samples form each group? If not, the number of the evaluated samples
should be indicated.
In the left panel of Figure 6, phosphor-p38MAPK was evaluated. Although statistical significance was obtained in reduced b2GPI-treated group, the difference in immunoblot is not impressive. At least, the amount of total p38MAPK should be similar between comparisons.

2) Discretionary Revisions
The mechanism of reduced b2GPI in decreasing LDL-c has not been addressed.

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.