Author's response to reviews

Title: The role of the C1q-gC1qR complex in regulating survival of human papillomavirus 16-infected cervical cancer cells

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Author's response to reviews: see over
Dear BioMed Central Editorial Team:

Thank you for your e-mail. Our manuscript (MS: 1716388942465724 The role of the C1q-gC1qR complex in regulating survival of human papillomavirus 16-infected cervical cancer cells) has been revised according to BMC cancer format suggestion.

Reviewer # 1:

Major revisions:

1) They used only one cell line, Hela, which is positive for HPV18 (high-risk type for cervical cancer). They did not mention why this cell line was chosen and whether their experiments are affected by endogenous HPV18 E6/E7. It is to be addressed why the exogenous HPV16, not the endogenous HPV18, shows the phenotype in their experiments.

-----Yes, you are right. In our experimental design, we have considered the effect of endogenous HPV-18 E6/E7 on cancer cells. Because the same cell line was used in present experiment, Hela cells transformed without exogenous HPV-16 E6 and E7 oncogenes was chosen control group.

2) Although HPV16 E6/E7 decreased the gC1qR induced apoptosis, the suppression level is modest. They should discuss why the apoptosis is not completely suppressed by the HPV16 E6/E7.

-----Yes. The discussion section has been demonstrated that the suppression of HPV-16 E6/E7 is nonspecific, so the expression of gC1qR is not completely suppressed by the HPV-16 E6/E7.

3) ‘Discussion’ section is not satisfactory. Most of the paragraphs, except for the last paragraph, are already mentioned in the sections of ‘Introduction’ and ‘Results’. Other roles of HPV E6/E7, other possible mechanisms to suppress gC1qR, phenotype expected by other types of HPV, and the general roles of gC1qR
(ubiquitously expressed) in normal tissues should be discussed. As well, they should mention that the immune evasion and anti-apoptosis are not simply explained by the suppression of gC1qR alone.

----According to reviewer's suggestion, ‘Discussion’ section have been elaborately rewritten.

4) Quality of written English is significantly poor. In addition to incorrect grammar and spelling, there are many inappropriate sentences in scientific papers.

----We revised the WHOLE manuscript carefully to avoid language errors. In addition, we consulted a professional language editing service to check the English via https://languageediting.elsevier.com/. We believe that the language is now acceptable for the review process.

Minor Essential Revisions

1) Figures are not properly numbered.

----Yes. The Figures have been arranged in a better way.

Discretionary Revisions

1) They could have chosen HPV-negative cervical cancer cell lines, such as C33a, in this study. It would be helpful to discuss whether endogenous HPV E6/E7 in HPV-positive cervical cancer cells might have some effect to suppress gC1qR mediated apoptosis.

----Reviewers suggestion is very important for us, in our next experiment, we would explore HPV-negative cervical cancer cell lines, such as C33a.

Reviewer # 2:

1) It is already known in other cell systems that, along with ROS generation, overexpression of gC1qR induces Ca2+ influx in mitochondria which leads to loss
of mitochondrial membrane potential, resulting in apoptosis. Meanwhile, E6 oncoprotein of HPV-16 degrades p53, which induces apoptosis through regulation of mitochondrial function. Hence, it is quite reasonable that E6 overexpression inhibits mitochondria-mediated apoptosis through downregulating the mitochondrial membrane protein gC1qR. However, this fact does not provide any evidence supporting the gC1qR-mediated “immune system” evasion by high-risk HPV oncoproteins.

-----In our introduction, we have quoted that gC1qR is the receptor for the globular heads of C1q, which mediated biological functiona by C1q-gC1qR complex on mitochondrial matrix. As we known, C1q is an important member in immune system, when E6 oncoprotein of HPV-16 downregulated the expression of gC1qR, the activation of C1q was affected, so we concluded that gC1qR mediated immune system.

Thanks for Editor’s help again. We wish that our reply will be satisfied for you and reviewers. By the way, we have corrected our manuscript according to BMC cancer format suggestion.

Please keep in touch with us. With our best regards!

Yu-zhu Peng, et al.

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