Author’s response to reviews

Title: The study of calcified atherosclerotic arteries: an alternative to evaluate the composition of a problematic tissue reveals new insight.

Authors:
Silvia FITTIPALDI (sv.fittipaldi@gmail.com)
Francesco Vasuri (vasurifrancesco@libero.it)
Alessio Degiovanni (alessiodegiovanni@gmail.com)
Rodolfo Pini (rudypini@gmail.com)
Mauro Gargiulo (mauro.gargiulo2@unibo.it)
Andrea Stella (andrea.stella2@unibo.it)
Gianandrea Pasquinelli (gianandrea.pasquinelli@gmail.com)
William G. Thilly (thilly@mit.edu)
Elena V Gostjeva (gostjeva@mit.edu)

Version: 2 Date: 22 Jun 2016

Author’s response to reviews:

Bologna, 22sd June 2016

Object: Revised manuscripts for BMC Clinical Pathology Submission

To the Editors,

Thank you for allowing us to correct and improve our manuscript entitled “The study of calcified atherosclerotic arteries: an alternative to evaluate the composition of a problematic tissue reveals new insight” by Silvia Fittipaldi, Francesco Vasuri, Alessio Degiovanni, Rodolfo Pini, Mauro Gargiulo, Andrea Stella, Gianandrea Pasquinelli, William G. Thilly and Elena V. Gostjeva. The
manuscript was changed according to the request. Modifications in the text are highlighted in red. Following the request of the editor, the abbreviations section was added to the manuscript and major details were furnished regarding the ethical approval section. In particular we clarify that all external IRB actions were also reviewed and approved by the Committee on the Use of Humans as Experimental Subjects and all were classified as "exempt".

Finally, as recommended, the dataset of raw data supporting the conclusions of the manuscript (referring to the table 2) was included as an Additional file 2. This spreadsheet includes the DNA quantity and the area of each single cell evaluated (for a total of 894 nuclei).

Please find below a point-by-point response to the comments.

1- Please provide all sections listed under the heading Declarations in our Submission guidelines.

Thank you for the remark, indeed the list of abbreviations was missing. I also added all the requested sections in the Declarations paragraph.

2- Please note that clinical data and personal details can only be shared if written consent to publish was obtained from all participants. This is a different form of consent than informed consent to participate in the study and it refers specifically to publication of personal information and details and must be obtained in writing. If consent to publish was not obtained, please state in your Availability of data and materials section that the data will not be made available in order to protect the participants’ identity.

In the manuscript no clinical data or personal details are furnished as all samples came from anonymous tissue discards. We never enrolled any patients in this study. As requested, we stated in the “Availability of data and materials” section that the data will not be made available in order to protect the participants’ identity. Only raw data concerning table 2 were furnished.

3- Please note also that any Declarations sections which are not applicable to your manuscript should still be included with the statement "Not applicable"

The sentence was added when appropriate.
4- We notice your study obtained samples not only from the US but also from hospitals in Europe. We would be grateful if you could let us know which European countries provided samples for this study and whether an IRB in every European country involved approved the study protocol in addition to the approval you have stated was obtained from the MIT ethics committee. Please confirm also whether the need for informed consent was also waived by an IRB in every European country involved. If ethics approval and exemption from informed consent were obtained from European IRBs, please clearly state this in your Ethics and consent to participate section of the References.

The receipt of human tissues at MIT was reviewed and approved as "anonymous tissue or tumor discards" by all participating medical facilities using structures (IRBs) that met the United States NIH guidelines at the time. This included the IRB established circa 2004 by the Greater Yalta Medical Consortium that communicated its structure and processes to the MIT IRB, which certified that they met US NIH standards. All external IRB actions were also reviewed and approved by the MIT IRB (Committee on the Use of Humans as Experimental Subjects (COUHES approval number 0804002679)) and all were classified as "exempt".

We received fixed samples of tissues as surgical discards from medical procedures unrelated to our research. These patients are anonymous to us. The MIT IRB reviewed these procedures and collaborating hospitals in advance of receiving any samples since 2004. According to you comment we modified the material and method sections and the Ethics approval and consent to participate.

5- Please place the Additional file section, currently located above the Competing Interests section, after the References.

As suggested we placed the Additional file section after the reference section.