

Author's response to reviews

Title: Understanding environmental causes of disease: what can we expect from new concepts and technologies?

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Author's response to reviews:

Dear Ms Herz,

Please find enclosed a revised version of the paper 1159452004242409 – “Understanding environmental causes of disease: what can we expect from new concepts and technologies?” (One copy with changes highlighted; one clean copy). We have incorporated all the changes suggested by the Editor and the reviewers.

Editor:

1. Key references have been added to support the premise of the commentary. The paper has also been restructured slightly, and the flow has been improved. Both the abstract and the conclusion have been modified.
2. Words used repeatedly, e.g. exciting, have been deleted or replaced.
3. The word ‘animals’ has been replaced with ‘laboratory animals’.
4. Page 8 – ‘susceptibility’ has been changed to ‘hyper-susceptibility’.
5. Page 8 – 50s has been changed to 1950s.

Reviewer 1: Martyn T Smith

1. We have improved the flow between the “–omics” section and the rest of the paper. We have discussed their potentials for the future in much detail, as well as the limitations and challenges we face in using “–omics” in environmental health. Two tables have been added for this purpose (tables 1 and 2). A more critical review has been incorporated.
2. Page 11 – The section on ‘genomics’ has been reworded. A section on ‘genotyping’ has been added with examples.
3. Page 11 – The sentence on ‘proteomics’ and ‘metabolomics’ has been modified.
4. Page 12 – Reference has been added.
5. Pages 12, 13 – Both sections have been revised. A more detailed discussion

on 'epigenomics' and 'proteomics' has been added.

6. Page 14 – We say that metabolomic profiling may be more amenable, as suggested, for example, by studies showing that the main yeast metabolome consists of fewer than 600 low-molecular-weight compounds. We added that it should be noted that the yeast has only 4,000 genes and is a unicellular organism, representing thus an oversimplified model to study humans.

Reviewer 2: Manolis Kogevinas

1. We have discussed more clearly the connection of all the technologies with the effect of low dose environmental exposures and clinical vulnerability. The main thesis of the paper has been substantiated with more explanations, along with figure 2.

2. The 'abstract' and the 'conclusion' have been modified.

3. Two tables, one with a summary of the “–omics” technologies, and the other describing the promises and limitations of –omics, have been added (tables 1 and 2).

4. Regarding 'new tools in exposure assessment, other than –omics', we have not included a part on exposure assessment technologies that do not belong to omics because that would require a whole different paper. We have decided to stick to new intermediate biomarkers.

5. Page 3 – grammatical corrections made.

6. Examples on benzene studies have been cut down. Other examples have been added.

We hope that the current version is acceptable for publication.

With kindest regards.

Paolo Vineis