Reviewer's report

Title: Effect of n-3 polyunsaturated fatty acid on gene expression of the critical enzymes involved in homocysteine metabolism

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Reviewer: Lydia Afman

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Within this manuscript the authors refer to literature which showed that omega-3 FA intake can result in a reduction of homocysteine levels. The authors would like to study the possible underlying mechanism. Therefore, they incubated HepG2 cells with 200 #M of different omega-3 FA and examined the expression of genes encoding enzymes involved in the Hcy metabolism and analyzed the FA concentration in the phospholipids membrane fraction in the cells.

The study is quite brief and several additional experiments should be done before any final conclusion can be drawn in studies with cell lines.

Major issues

A major drawback of the study is the use of cell lines, the questions remains whether the cell lines are good indicators of the liver. Furthermore the reason why this liver cell line is chosen is not explained.

Another point of concern is the way the FA were administrated to the cells, this is not clear from the methods.

The authors studied the cells after 48 hours and claim “The changes in PL fatty acid composition of cell membrane are likely to account for the changes in mRNA expression of the critical genes involved in methionine metabolism”. However, it is known that FA can activate gene transcription within a few hours via among other the PPARs, which means that you don’t necessarily need incorporation within the cell membrane to obtain such effects. If the transcription is regulated via the PPARs, the genes are likely to contain a PPRE binding site. This is however not studied.

If the FA really result in a reduction in Hcy levels one might expect a reduction in Hcy levels in the cells and if measurable also in the medium. A determination of Hcy levels would be of additional value.

Level of interest: An article of limited interest

Quality of written English: Acceptable

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

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