Reviewer’s report

Title: Polymorphisms in the mitochondrial oxidative phosphorylation chain genes as prognostic markers for colorectal cancer

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Reviewer: Peter Söderkvist

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This paper deals with an important feature for most tumor cells, to switch glucose fermentation for energy production from an efficient glycolysis and oxidative respiration to a less efficient way of ATP production, despite the presence of oxygen, i.e. the Warburg effect. Even though mitochondrial defects are rare in cancer and multiple mechanisms promotes glycolysis in cancer cells, genetic variations in the genes in the oxidative phosphorylation may still be an important mechanism for tumor progression. The authors selected from gene expression meta-analysis several candidate genes and potentially functional SNPs to study susceptibility for CRC progression.

This is an interesting study, indicating that genetic polymorphisms influence individual susceptibility for tumor progression. The study design is sound, the analytical methodology is relevant and the results are interesting.

However, there are some issues that needs to be addressed before publication.

Major Compulsory Revisions

SNP’s representing genes involved in all five protein complexes of the oxidative respiratory chain, except Complex II, are selected. Why are these genes not considered in this study, since they are argued (in Introduction) to be important for the Warburg hypothesis.

The difference of risk between colon and rectum are not discussed in mechanistic terms (table 4). Please provide an explanation and omit table 4. The results can be included in the text.

In table 6, a significant gene dose dependent effect is expected for rs 6510502 and rs10420252 and Tumour stage/ lymph nodes/metastasis, but not found. How come? A chance finding?

The Kaplan-Meier curves: It is not stated in the figure or legend, whether the length (x-axis) of the follow-up period represents days, weeks or months. Please clarify!

If they represents weeks, it is to short follow-up, since many patients are still alive. This figure can be omitted, since most information is already available in the tables.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

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