Reviewer’s report

Title: ARLTS1 polymorphism is associated with an increased risk of familial cancer: evidence from a meta-analysis

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Reviewer: Cecilie Heramb

Reviewer's report:

The paper presents a thorough study, and what must have been a labour-intensive metaanalysis.

Introduction: The nomenclature for the variants/polymorphisms should be HGVS - standard if you are discussing sequence variants or rs-positions if you are discussing SNPs. The reason for using the chosen nomenclature should nevertheless be stated. (Earlier studies have used it etc.) Definitions of genetic normal variation, SNPs vs genetic susceptibility alleles and disease-causing variants should be mentioned.

Method and material:

The methods for the meta-analysis and the statistical tests are described thoroughly and nice. I can't however fully review the statistics for this type of study.

Results: "Characteristics of included studies", should be placed in Methods- chapter? A forest plot to show previous results from the chosen studies would be nice.

Discussion: Some discussion on the difference in significance between nonsense mutation Trp149 Stop, and the other four variants which are missense could be included. (shown in table 4) The fact that polymorphisms in ARLTS1 leads to different types of cancer, but with altogether low risk estimates, 1.27 (1.15-1.41) for Cys148Arg CC, should be elaborated on. On its own this polymorphism is only a weak cancer risk factor, but may contribute in carcinogenesis in a way that is common for different cancers.

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An article of limited interest

Quality of written English
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Not suitable for publication unless extensively edited
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