Reviewer's report

Title: Genes involved in muscle contractility and nutrient signaling pathways within celiac disease risk loci show differential mRNA expression

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Reviewer: Lude Franke

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The authors describe an analysis of differential gene expression in celiac disease patients compared with healthy controls. They concentrate on genes that map with loci that have been previously established or implicated in celiac disease. While nearly all previously identified genome-wide significant celiac disease loci (that used a case control design) could be replicated, this has not been shown for the sib-pair GWAS loci and loci identified through linkage analysis. I suggest the authors concentrate on the established loci (identified through case-control GWAS), and omit the genes that map elsewhere.

Major compulsory revisions:

The authors need to make it explicit how many of the genes map within loci that have been found in celiac disease genome-wide association studies with significance < 5 x 1e-8. This particularly holds for the 4 SNPs for which the authors show an eQTL effect. How many of the Dubois et al 2010 NG paper eQTL genes were studied here, and how many of those showed differential expression?

Why did the authors not use microarrays? I think this might have been cheaper than running Taqman assays for 123 different genes. Additionally, it would have allowed for correcting the data for potential technical and biological confounders (e.g. batch effects), by using PCA and identifying such (hidden) confounders.

Selection criteria of these genes seem ad hoc: The authors included genes from a two-locus interaction test. Did the authors previously identify two-locus interactions? And could those interactions be replicated? The authors used two pathway enrichment methods (Ingenuity Pathway Analysis and Genetrail) to further select genes from certain enriched pathways (which are these pathways?). However: Doesn't that result in circular reasoning? You find enriched pathways, start analysing these, and whatever the outcome will subsequently conclude there is enrichment. How did the authors ensure this did not lead to any bias on the reporting and discussion?

Level of interest: An article of limited interest

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.

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