Reviewer’s report

Title: Comparison of DNA methylation profiles from saliva in Coeliac disease and non-Coeliac disease individuals

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Reviewer: Stephen Brown

Reviewer's report:

This manuscript reports a comparison of DNA methylation profiles from saliva in coeliac disease and non-coeliac disease individuals. The authors used the Illumine InfiniumMethylation450 Beadchip array to assess methylation in a series of 31 subjects with coeliac disease as well in 28 matched controls. Pyrosequencing was used to interrogate three cg sites in a second cohort of 148 subjects with coeliac disease and 73 controls. Importantly, the coeliac disease group had all been treated with a gluten free diet for a minimum of 2 years prior to study. The goal of the study was to identify stable genomic methylation changes in people with coeliac disease, with the hope that methylation differences might lead to insights into pathogenesis of coeliac disease or might provide useful biomarkers.

The cases are carefully and thoughtfully characterized, as are the controls. The methylation studies themselves seem to have been competently done and appropriately analyzed. In the initial study group, the authors report some statistically significant methylation differences between cases and controls; however, what is most remarkable is how few and how modest the differences were. Interestingly, the validation cohort, in which just 3 loci were analyzed with pyrosequencing, the initial results were not confirmed.

Overall, I see this as an interesting and well done study, with essentially negative results. Even though results are negative, it will be of interest. I have just a couple of specific comments:

When speaking of underlying SNPs that affect methylation results, the authors could be a bit more clear.

Along the same lines, figure 3 raises some questions. It appears that each of the 3 cg loci has a bimodal (or trimodal) distribution of methylation. It would be helpful if the authors would comment on this. If all three loci are affected by the presence of an underlying SNP, it would be very important to discuss.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
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Yes

Are the conclusions drawn adequately supported by the data shown?
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