Reviewer's report

Title: A novel sero-genetic approach determines the community prevalence of celiac disease and informs improved diagnostic pathways

Version: 1 Date: 15 June 2013

Reviewer: Umberto UV Volta

Reviewer's report:

The present paper describes a novel sero-genetic approach for detecting celiac disease (CD) avoiding unnecessary upper gastrointestinal endoscopy and duodenal biopsies in many cases with an isolated tTGA positivity, but without a genetic predisposition to CD.

I have only some comments, but not substantial issues:

1) Up to now in the current clinical practice, the positivity for tTGA of IgA class, found in screening studies in the general population, needs to be confirmed by EmA positivity before making an intestinal biopsy. Positivity for tTGA IgA (especially at a low titer) without EmA is regarded as a false positive result and patients with this antibody pattern do not usually undergo an intestinal biopsy, but they do have a serological follow-up. So, we agree that the proposed protocol with HLA typing is a step forward for excluding immediately CD, but it is undoubtedly more expensive than the previous one and not applicable everywhere. The Authors should underline that such a protocol can work only in countries with a florid economy.

2) The Authors employ a plenty of antibody tests, some of them probably not indispensable for routine use. Are all the tests included in this study (tTGA, tTGA/DGP IgG, DGP IgA, AGG, AGA, EmA) requested in the clinical practice or we can spare some tests also in order to reduce the costs for CD screening? In my opinion we can have good results by using tTGA of IgA class and DGP of IgG class as first step and EmA IgA as confirmatory test in positive cases. DGP of IgA class, AGG, AGA have a very low specificity as reported in literature. The Authors should indicate an antibody flow-chart for practical investigation.

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