

# Association of TNF- $\alpha$ -308G>A polymorphism and celiac disease

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Dear Editor, we read the publication on “Association of TNF- $\alpha$ -308G>A polymorphism with susceptibility to celiac disease: a systematic review and meta-analysis” with a great interest<sup>(1)</sup>. Aflatoonian et al. concluded that “the TNF- $\alpha$ -308G>A polymorphism plays an important role in celiac disease susceptibility. However, our results are still needed to strengthen by further studies in different ethnicities and larger sample sizes<sup>(1)</sup>”. We would like to share ideas on this report. First, it is agreeable that a larger sample sizes of subjects are require to strength the conclusion. Nevertheless, we should not forget to recognize the effect of other genetic polymorphisms that might result in susceptibility to celiac disease (such as 174 G/C and -572 G/C of IL-6 gene polymorphisms<sup>(2)</sup>).

In fact, the genetic change from G to A can result in alteration of molecular structure. If we apply molecular quantum calculation to assess the molecular change, according to methods used in the previous referencing studies<sup>(3-5)</sup>, the molecular weight at variant position due to G to A genetic variation decreases up to 16 g/Mol (from 151.13 to 135.13 g/Mol) This means the required number of molecule per final phenotypic expression of TNF- $\alpha$  in A allele is less. Since TNF- $\alpha$  is well-described for its immunopathogenic role, enhancing the IFN-gamma-induced increase of HLA-class II expression on surface enterocytes in celiac disease, the more expression per Mol in A allele can explain an increased risk in TNF- $\alpha$ -308G>A polymorphism.

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