Review of: "Genome-wide pharmacogenetics of anti-drug antibody response to bococizumab highlights key residues in HLA DRB1 and DQB1"

Ghasem Solgi

Potential competing interests: The author(s) declared that no potential competing interests exist.

Dear Editor

Thank you for your kind invitation and sending an interesting paper on GWAS in relation to ADA and HLA genes linkage. Below is some comments that might be useful for authors and readers of this paper.

1. The first strength is a reasonable classification of the study population into five measures based on ADA status and NAbs.
2. performing conditional analysis to find out index SNPs in the MHC region is also interesting and comprehensive.
3. There is a typing error in fig. 1 legend: anti-body must be antibody.
4. Data presented in fig. 2 has not been discussed in terms of the importance of AA variant in DQB1_71 and its relation with ADA titre in top 10%.
5. Genetics of longitudinal ADA titer: Also, this part is missing in the discussion and author didn't imply or discuss the significant lead variant for ADA status or ADA titer or NAb positive status in different time intervals (week 12 and week 4).
6. Discussion lacks a meaningful interpretation for no association between changes in LDL-C levels and potential genetic variants in relation to ADA status.
7. The authors highlighted the critical residues in the MHC molecule and even some confirmed residues in several autoimmune diseases (e.g aa in SE alleles in RA, residues in T1d and SLE). I think, discussing the DRB1 13 residue which is shared between above mentioned diseases and appearance of ADA maximum titer in the current study may lead the readers to define a critical residue rather than haplotypes in developing auto antibodies particularly against mAbs.

Sincerely

Ghasem Solgi