anti-TNF medications in MS?

(1) be associated with lower disease activity/severity

(2) reduce the requirement for anti-TNF therapy

(3) influence the efficacy of anti-TNF therapy in AS.

In this manuscript, Dr. Vecellio et al have conducted a comprehensive evaluation to the effect of genetic polymorphism rs1800693 in TNFRSF1A to AS disease activity/severity and anti-TNF therapy in a quite large Caucasian cohort. The authors tried different strategies and different outcome index and demonstrated rs1900693 exerted no influence on either the intention to treat with or efficacy of anti-TNF treatment. The study was performed rigorously, and the findings are quite interesting. I only have several suggestive comments to the manuscript.

**Major Compulsory Revisions**

1, In the first part of result, BASDAI section, whether [Multicollinearity](https://en.wikipedia.org/wiki/Multicollinearity) has been checked? Relevant colinear variables could be removed in the linear/logistic regression and then check about the direction of the GG/AA to BASDAI.

2, The authors tried to evaluate the relationship between rs1800693 and anti-TNF treatment, it is a good idea. However, how about just trying to build a prediction model based on the variables in the current study. Then report the prediction accuracy, sensitivity and specificity, especially with the procedure of dexterously feature selection.

**Minor Essential Revisions**

1, The title of the manuscript can be shorted, such as replace tumour necrosis factor receptor with TNFRSF1A.

2, Although no positive association was identified, it is better that the authors could provide the result (Table) of the section: BASFI and BAS-G as well as Anti-TNF therapy as the supplementary Tables.

**Discretionary Revisions**

1, In my opinion, this samples are quite valuable, and the authors also mentioned that there are 100+ polymorphism which are related with AS, why only genotyping rs1800693. If I were you, I would genotype all these polymorphisms and identify the most positive SNPs. Or the authors already genotyped some other SNPs while this manuscript is the paper in the first phase?