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**Name of Journal:** *World Journal of Hematology*

**ESPS Manuscript NO:** 27052

**Manuscript Type:** ORIGINAL ARTICLE

**Manuscript Title** Identifying changes in Punitive Transcriptional Factor Binding Sites from rSNPs that are significantly associated with Disease or Sickness

**Reviewer's comments:** I thank the reviewers for their helpful comments. I have addressed all of their corrections and revisions and made the appropriate changes in red lettering throughout the manuscript.

**Reviewer #** 00646254

**Major comments:**

1) In Abstract, there is no conclusion. Please add the conclusion to end region of Abstract.

*A concluding sentence has been added to the end of the Abstract.*

2) You should explain the meaning of "punitive" word for scientists of other fields in introduction section.

*This has been changed to "punitive or potentially".*

3) You should more explain how you can define unique TFBS.

*In the Introduction, I have added an example of unique TFBS from Table 2 to illustrate the unique TFBS difference between SNP alleles.*

4) If you are not using CHIP (TF-Chromatin binding site) assay or references, you should use letter, 'potential or putative TFBS' in content of manuscript as well as table.

*This has been done throughout the manuscript and table headings.*

5) You should explain what is unique TFBS is mean in Introduction by using general examples, if this finding is important in your study.

This has been done and an example has been used. See response to comment 3 above.

6) Please explain the reason why this study performed with rSNPs within only nine genes.

This has been addressed in the first sentence of paragraph two of the Introduction stipulating that this study is only a subsample of the human genome which states that “In this report, rSNPs within a sample of nine human genes (Table 1)”.

Minor comments:

In abstract,

- 1) The genome-wide association studies (GWAS) **has** was changed to **have**
- 2) enhancers has been changed to **enhancers** (This has been done throughout the manuscript).
- 3) TFBS has been written out as **transcriptional factor binding site (TFBS)** on its first occurrence in the manuscript.

In Introduction.

- 1) The genome-wide association studies (GWAS) **has** was changed to **have**

In Discussion,

- 1) these rSNPs Tables 2 & 3) has been changed to these rSNPs Tables (2 & 3)

**Reviewer # 00340828**

Without experimental confirmation, the emphasis could only be limited to theoretical prediction.

This has been emphasized throughout the manuscript when the words “punitive” or “potential” TFBS is used.

Instead of using only one sentence at the end of the Discussion to briefly carry it over. For example, are there publications present experimental results in support to computational predictions?

At this point, in this type of research, there are not many references; however, I do include one such reference and include an additional sentence dealing with ChIP-seq as a method for validating future computational studies including references to support this direction.