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Receipt of reviewer's report for SREP-16-04775

1 message

scientificreports@nature.com <scientificreports@nature.com> Mon, Mar 21, 2016 at 12:41 AM
Reply-To: scientificreports@nature.com
To: scguo@ucsd.edu

Dear Dr Guo,

Many thanks for submitting your referee report on "Identification of a Functional SNP rs17079281 at 6q22.2 Locus That Is Associated with Lung Cancer Risk" by Prof Qian. We appreciate the time you have taken to review this manuscript for Scientific Reports. A copy of this report is attached below for your reference.

Best regards,

Manuscript Administration
Scientific Reports
4 Crinan Street
London N1 9XW
E-mail: scientificreports@nature.com

Is the manuscript technically sound?: Yes

Could the manuscript become technically sound with revision?: Yes

Are the conclusions supported by the evidence presented?: No

Are additional experiments or data required to support the conclusions?: Yes

Does the manuscript only duplicate previous work?: No

Appropriate use of statistics and treatment of uncertainties?: Yes

References: appropriate credit given to previous work?: Yes

Is the manuscript written clearly using Standard English?: Yes

Electrophoretic gels and blots are presented clearly and are free from apparent manipulation?: N/A

Technical Comments to the Author:

Recommendation: Major Revision

Remarks to the Editor:

Remarks to the Author:

Comments to the Authors,

Dr. Wang conducted a genetic case-control association study and further biological validation to demonstrate a functional SNP which is highly linked with the GWAS identified NSCLC associated SNP were involved with cancer susceptibility by influencing the binding of transcript factor YY1. The idea and the strategy were excellent and it would give a great help to understand the interaction between SNP and TF binding in the complex disease susceptibility. However, I still have several consideration on the study design and the statistic method.

Major Compulsory Revisions

1, The author estimated the LD between GWAS SNPs with other adjacent SNPs with Hapmap dataset, However, 1000 Genome data have been released several years ago, the LD block analysis to 1000 Genome data would be more powerful to detect more SNPs with is linked to the interest SNP in this study.

2, In the association study, as an accurate study design the smoking, BMI between case and control population should be almost same or no significantly difference so that the genetic difference could be estimated. Why the authors didn't control these confounders? Do you think these effects can be adjusted 100% with the statistic model? What's worse, I cannot understand why the author show the Chi-square P-value in Table 3, rather than logistic P-value? Finally, although the number of candidate SNPs in the study were not too many, the P-value will turn not to be significant after multiple test correction.

3, It is still very difficult to understand the logic of the study. Such as 1) YY1 is low expressed in lung cancer cell lines. 2) Expression of DCBLD1 was not significantly different among different genotypes, even though the authors gave several hypothesis. 3) Another difficult question is that for the SNPs or genotype, the distribution was only little different between cancer and normal population and you can find the proportion of the genotype was almost very close, even the P-value was significantly, in such way, the molecular function interpretation should be carefully. I suggest that the eQTL analysis can be repeated again with large sample size to check whether the difference between different genotype were significant, if so, then everything is clear, or else, the author should be give more comprehensive and reasonable explanation.

Minor Revisions

1, In table 2, the location of the SNPs should be shown and the order should be same with the genomic position order.
2, In table 3, the test should be adjusted with BMI, Smoking, gender and age.
3, In Figure 2B, the scale should be provided.
4, Figure 2C, the location of the star should be changed.