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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Translational Medicine
ESPS manuscript NO: 21996
Title: Potential therapeutic targets from genetic and epigenetic approaches for asthma
Reviewer's code: 00503929
Reviewer's country: Brazil
Science editor: Shui Qiu
Date sent for review: 2015-08-07 16:34
Date reviewed: 2015-10-01 01:31

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

REFEREE'S COMMENTS TO AUTHORS This is a well-organized and authoritative review on a timely subject, which is entirely pertinent to the field of Translational Medicine. The authors have reviewed an extensive body of literature on genetic and epigenetic markers which were found to be associated with the asthmatic phenotype, and make the case that many of the more strongly associated markers are good candidates for therapeutic intervention. There are few scientific mistakes in the paper, but they are significant and must be corrected (see below). On the other hand, there are numerous examples of inappropriate usage of English, which equally require thorough revision by someone fully familiar with English grammar and scientific usage of English. Both types of corrections are essential to make this manuscript as useful as it should be to the Journal's readerships. Scientific issues: Page 4: "DNA methylation involves the addition of a methyl group to the DNA nucleotide cysteine and adenine which lead to gene silencing". Please correct this phrase, as cysteine, an aminoacid found in proteins but not in DNA, is obviously NOT a nucleotide. I assume the author meant cytosine, which I understand to be a nitrogen base which is part of nucleosides and nucleotides, just like adenine, but is not a nucleotide. nucleotide itself. This mistake is at odds with

the rest of the text, which shows familiarity with the terms of genetics, and must be corrected. Page 6: D19 (+) B lymphocyte methylation patterns. Unless I am thoroughly mistaken, the author means CD19 (+) B lymphocyte. The missing "C" may not seem much, but in a world full of novel gene names and markers, some reader might think D19 (+) is something newly discovered rather than a very well established marker for B lymphocytes. If it is CD19, the sentence makes sense; if it is not, I don't understand what it means, as "D19" is not defined anywhere in the paper. Please note that the manuscript, as expected, deals with hundreds of gene and gene products which are not defined in a list of abbreviations. Since most of them are only known to specialists, there is real risk of confusing the nonspecialist reader when a term is used only once, and especially if it is an acronym without a definition. Page 13 and elsewhere, use of interleukin nomenclature: interleukins are a class of cytokines, and as such are gene products (proteins) rather than genes. Official interleukin nomenclature includes hyphenation (e. g.: IL-33, IL-18 and IL-1). I understand the nomenclature for the corresponding genes may dispense with hyphenation and present letters and numbers in italics (e.g. IL18R1). The paper deals with both genes and gene products but sometimes confuses the reader by not using the mandatory hyphen when a protein is meant. This confusion must be avoided, especially considering the complexity of the issues, which can easily give rise to misunderstandings. Language issues. Missing words, sometimes several in a single sentence; incorrect spelling in a few cases; and inappropriate use of some terms contribute to make the text difficult to read. I strongly recommend thoroughly reviewing this manuscript as to language and clarity so as to make it in form as good as an authoritative review should be.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Translational Medicine
ESPS manuscript NO: 21996
Title: Potential therapeutic targets from genetic and epigenetic approaches for asthma
Reviewer's code: 00432161
Reviewer's country: Singapore
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Date sent for review: 2015-08-07 16:34
Date reviewed: 2015-08-20 10:19

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Overall this review has covered most of the recent GWAS studies and miRNA works associated with asthma. 1. The current review is mainly focused on the anti-inflammatory aspect. There are quite a few genomic and epigenetic studies related to lung function not cited. I encourage the authors to discuss the following references: Covar RA et al. (2004) Childhood Asthma Management Program Research Group. Progression of asthma measured by lung function in the childhood asthma management program. Am J Respir Crit Care Med 170:234–241. Hirota T et al. (2011) Genome-wide association study identifies three new susceptibility loci for adult asthma in the Japanese population. Nat Genet 43:893–896. Repapi E et al. (2010) Wellcome Trust Case Control Consortium; NSHD Respiratory Study Team. Genome-wide association study identifies five loci associated with lung function. Nat Genet 42:36–44. Hancock DB et al.(2010) Meta-analyses of genome-wide association studies identify multiple loci associated with pulmonary function. Nat Genet 42:45–52. 2. There are also targets identified by other genomic approaches and meta analysis, which can be discussed under the current title. The authors should refer to the following papers: Despotovic M et al. (2015) Gene polymorphisms of tumor necrosis factor alpha and antioxidant enzymes in bronchial asthma. Adv

Clin Exp Med 24:251-256. Huang H et al. (2014) Effects of TNF-α polymorphisms on asthma risk: a systematic review and meta-analysis. J Investig Allergol Clin Immunol 24:406-417. Yang G et al. (2014) Association between tumor necrosis factor-α rs1800629 polymorphism and risk of asthma: a meta-analysis. PLoS One 9:e99962. 3. It is quite established IL-17 family members such as IL-17A/F and IL-17E (IL-25) are essential to asthma pathogenesis, especially severe asthma. Were there any GWAS study regarding IL-17? There are studies showing positive association between IL-17A/F polymorphism and asthma. IL-25 receptor IL-17RB gene polymorphism is also associated with asthma. The authors can incorporate IL-17 family member relevant information into the review. Jung JS et al (2009) Association of IL-17RB gene polymorphism with asthma. Chest 135:1173-80. Hunninghake GM et al. (2011) The CD4+ T-cell transcriptome and serum IgE in asthma: IL17RB and the role of sex. BMC Pulm Med 11:17 Schieck M et al. (2014) Genetic variation in TH17 pathway genes, childhood asthma, and total serum IgE levels. J Allergy Clin Immunol 133:888-91. Maalmi H et al. (2014) IL-17A and IL-17F genes variants and susceptibility to childhood asthma in Tunisia. J Asthma 51:348-54. Park JS et al. (2013) Association of single nucleotide polymorphisms on Interleukin 17 receptor A (IL17RA) gene with aspirin hypersensitivity in asthmatics. Hum Immunol 74:598-606. 4. In the "traits" column in table 1 and 2, it lists asthma/lgE/lung function. Please explain.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Translational Medicine
ESPS manuscript NO: 21996
Title: Potential therapeutic targets from genetic and epigenetic approaches for asthma
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Reviewer's country: Greece
Science editor: Shui Qiu
Date sent for review: 2015-08-07 16:34
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[Y] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

A well written review that summarizes the current knowledge on the genetics of asthma. An editing of the text for minor corrections in syntax, grammar and reference input is appropriate.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Translational Medicine
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Reviewer's country: China
Science editor: Shui Qiu
Date sent for review: 2015-08-07 16:34
Date reviewed: 2015-10-02 20:44

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[Y] Accept
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
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		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This ariticle makes a comprihensive review on recent epigenetic approaches including DNA methylation and chromatin modification on histones in asthma and IgE, and micro RNAs in asthma.Therefore, it provides new therapeutic means for clinical management of the disease in future.