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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35702

**Title:** Genetic Associations with Adverse Events from anti-TNF therapy in IBD patients

**Reviewer's code:** 03658321

**Reviewer's country:** Sweden

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-08-05

**Date reviewed:** 2017-08-07

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

Thank you for the interesting and well done study. The paper is well written, but an issue needs further development. As your result show that IgA ASCA is associated with lower risk of any adverse event to anti TNF, I would like you to include in discussion section a proposed mechanism for this interaction. The same regarding Anti I2 in UC patients, where anti I2 were associated with infusion reactions.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35702

**Title:** Genetic Associations with Adverse Events from anti-TNF therapy in IBD patients

**Reviewer's code:** 02440884

**Reviewer's country:** Germany

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-08-08

**Date reviewed:** 2017-08-08

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

The study includes 1,258 patients (954 CD, 260 UC, 44 IBDU) and 21% were found to have adverse events to anti-TNF-alpha therapy. In CD IgA ASCA was identified as potential biomarker. Comments 1. A subgroup analysis is necessary. Is there any evidence that CD includes an anti-TNF-alpha sensitive group with an increased rate of adverse events? Can you characterize this subgroup by clinical or molecular parameters? 2. The IBDU patients should be analyzed in more detail. The frequency of events should be correlated with CD as well as UC patients. Is there any re-classification possible?

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35702

**Title:** Genetic Associations with Adverse Events from anti-TNF therapy in IBD patients

**Reviewer's code:** 01220198

**Reviewer's country:** United Kingdom

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-08-08

**Date reviewed:** 2017-08-09

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

## COMMENTS TO AUTHORS

Congratulations on this interesting study. My only suggestions is to shorten the introduction and discussion and highlight the genetic results in the conclusions

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35702

**Title:** Genetic Associations with Adverse Events from anti-TNF therapy in IBD patients

**Reviewer's code:** 02446483

**Reviewer's country:** Canada

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-08-08

**Date reviewed:** 2017-08-10

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

## COMMENTS TO AUTHORS

A retrospective chart review was done of patients attending the IBD centres at Cedars-Sinai IBD Centre from 2005 to 2016. This study was done to describe the type and frequency of adverse events associated with anti-TNF- $\alpha$  therapy in patients diagnosed with Inflammatory Bowel Disease (IBD) in a large cohort and to evaluate for any serological and genetic associations. This study was warranted because there are few studies documented that investigate the adverse effects of anti-TNF- $\alpha$  therapy. The research group were able to cover their objectives and addressed the adverse events associated with therapy. A relatively large study population was used compared with study populations used in similar studies in the past. The findings from this study would go towards helping to reduce the adverse effects of therapy and would give more patients a better chance of improve compliance and tolerance to anti-TNF- $\alpha$  therapy. Major Issues 1. The researches indicated that the overwhelming majority of the patient population studied was of European ancestry. No mention was made of what



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percentage of patients was of European ancestry. IBD is known to affect all racial groups, so the population studied did not fully represent the patient population of IBD as minority groups were definitely underrepresented in this study. The paper did not mention the reason for this variation in the study group. This is most likely due to the Cedars-Sinai Medical Centre being located in the predominantly Caucasian neighbourhood of Beverly Grove, Los Angeles, California. The ethnic demographics are not typical of the multicultural Los Angeles. Correlation of results with a study done in a more multi-ethnic medical centre would have been valuable. In conclusion, this paper was informative and the authors described clearly the methodology used and results which were obtained. Limitations in the study, as well as, recommendations such as the need for further research were addressed.