

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 34606

Title: Circulating miR-125a but not miR-125b decreases risk of active Crohn's Disease and negatively correlates with disease severity as well as inflammatory cytokines

Reviewer's code: 00503587

Reviewer's country: New Zealand

Science editor: Ze-Mao Gong

Date sent for review: 2017-05-12

Date reviewed: 2017-05-24

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 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 checked="" 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 checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" 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

This work focused on two mRNA molecules and their potential relevance to IBD

Specific Comments

1. The title requires revision. It states a decreased risk of active CD. This could mean a decreased risk of a flare of disease, or a change in this marker during active disease or a decreased risk with the development of CD. It should be revised to be more clear and accurate
2. The Methods section of the ABSTRACT contains numbers that should be in the Results section
3. There are numerous errors of English language (grammar and word usage) in every section of the work that all require correction
4. What is meant by a converse association (ABSTRACT)?
5. The word "dramatically" would be better replaced with a word more suitable to a scientific publication
6. The ABSTRACT comments on 3 months of treatment, but does not specify the nature of this. Later in the RESULTS section, this is also not well described
7. The INTRODUCTION suggests a direct relationship between GDP and development of IBD. Is this

well-documented? If so, an appropriate reference should indicate this 8. The INTRODUCTION includes the abbreviations of terms (e.g. NF-kB) without explanation of the full term 9. Any company that was the source of reagents should be provided with full details (as per standard protocol) 10. Were the cytokines also measured in the control patients as well? This is not indicated 11. One outcome was repeat assessment of CDAI at 3 months. Were bloods 9as more objective assessments) not measured at this time? 12. It is unclear what a "great diagnostic value" is (Results). This should be revised. 13. The DISCUSSION suggests that this is a retrospective study, yet the methods appears to indicate prospective recruitment, and subsequent assessment of key outcomes. This should be corrected/consistent 14. The titles/legends for Table 1 and Figure 1 should be revised to include more specific details (so that they are more independent of the text of the MS) 15. Some of the Figures (e.g. on Fig 4) contain unhelpful negative data - is this necessary? Inclusion as negative results in the text of the RESULTS section may be adequate (with a supplementary online table if required)

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Manuscript NO: 34606

Title: Circulating miR-125a but not miR-125b decreases risk of active Crohn's Disease and negatively correlates with disease severity as well as inflammatory cytokines

Reviewer's code: 02618027

Reviewer's country: United States

Science editor: Ze-Mao Gong

Date sent for review: 2017-05-12

Date reviewed: 2017-05-25

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 checked="" 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 type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
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		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Crohn's Disease (CD) is an important clinical problem, and microRNAs have been shown to be implicated in the inflammatory bowel seen in CD. Decreased levels of miR-125a were found in the plasma of patients with active CD (A-CD), compared to patients with remission CD (R-CD) or healthy controls (HC). However, circulating miR-125b levels remained unchanged between patient groups. While the results are interesting, several concerns are noted: Major comments: 1. What tissue or cell type might be the largest contributor of miR-125a in the circulation of HCs? 2. What are the differences between miR-125a and miR-125b that may be responsible for the dichotomy of the observations seen in A-CD and R-CD? 3. What were the circulating levels of miR-29b, let-7, miR-192, miR-142-3p, miR-21, miR-495-5p, and miR-19b in A-CD, compared to R-CD and HC patients in this study? Do any of those miRs also correlate with severity of CD and inflammatory cytokine expression? 4. How was plasma

extracted from blood? The centrifugation details are important to ensure that red blood cell lysis has not occurred to contaminate the plasma samples used for analysis. 5. How did the cytokine levels of IL-17, TNF α , and IFN γ in R-CD patients compare to HC? 6. Do miR-125a and miR-125b have different targets? 7. Were levels of Tregs and TH17 measured in the plasma collected? Since miR-125a correlated with severity of CD, did Tregs and Th17 (known targets of miR-125a) also correlate with severity of CD? Minor comments: 1. The manuscript text should be reviewed for proper use of grammar and syntax. 2. Contractions should not be used in formal scientific publications, e.g. "didn't" (Abstract Results) and "couldn't" (Results). 3. CRP, CDAI, IL-17, TNF- α , IFN- γ , etc. should be defined in the Abstract. 4. If used only once in the text, an abbreviation is unnecessary, e.g. "(GDP)" is not needed after "gross domestic product". 5. CRP, ESR, and CDAI should be defined in the Materials and Methods.