



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 35987

**Title:** miR-192-5p regulates lipid synthesis in non-alcoholic fatty liver disease through SCD-1

**Reviewer's code:** 00607646

**Reviewer's country:** Argentina

**Science editor:** Li Ma

**Date sent for review:** 2017-09-11

**Date reviewed:** 2017-09-13

**Review time:** 1 Day

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**

The MS entitled "miR-192-5p regulates lipid synthesis in non-alcoholic fatty liver disease through SCD-1" by Liu X-L et al about the regulation of lipid synthesis in NAFLD through the effect on SCD-1 is timely, novel and well-written though with some problem of citations. The order of some cites should be altered conserving the order of the original contributions. Reviews should be avoided in particular when cites referred to main issues. In the introduction, 1-The association of NAFLD with mitochondrial dysfunction has been amply documented, and it was even related to epigenetic changes (Pirola et al., 2013)(Silvia Sookoian et al., 2016)(S. Sookoian et al., 2016)(S. Sookoian et al., 2010). 2- the role of miRs in NAFLD was found by many groups no cited in the introduction. In particular, the increase of miR-122, 194 and 34 in patients with NAFLD was previously described (cite 19), even before the citation 9 of the own authors. The



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power of discriminating between control, NAFL and NASH was also described in that work (cite 19). Please rephrase and cite the previous work properly in the introduction but also in the discussion, where proper credit should be given to the previous work. Please provide the rationale to use liraglutide as a treatment group. In addition, control group treated with liraglutide might be recommended, please explain. As the effect of liraglutide may be associated with the impairment of body weight gain, it would be important to adjust the differences in miR-192 expression and SCD-1 levels for and equivalent BMI in the rat, such as body weight divided by the distance between nose and tail. As the experiment is already performed, the body weight, although imperfect may be used. The mimics and anti-miR used are poorly described. Please provide more details. If the sequence is known add it to the MS. In the case, it is commercially protected, provide more details as to how to obtain them. The qPCR are also poorly described, and more details about the specific assay should be provided. There are some typos, i.e. Kuels is Keuls. please revise. References suggested: Pirola, C. J., Fernandez Gianotti, T., Burgueño, A. L., Rey-Funes, M., Loidl, C. F., Mallardi, P., ... Sookoian, S. (2013). Epigenetic modification of liver mitochondrial DNA is associated with histological severity of nonalcoholic fatty liver disease. *Gut*, 62(9). <https://doi.org/10.1136/gutjnl-2012-302962> Sookoian, S., Castaño, G. O., Scian, R., Gianotti, T. F., Dopazo, H., Rohr, C., ... Pirola, C. J. (2016). Serum aminotransferases in nonalcoholic fatty liver disease are a signature of liver metabolic perturbations at the amino acid and Krebs cycle level. *American Journal of Clinical Nutrition*, 103(2). <https://doi.org/10.3945/ajcn.115.118695> Sookoian, S., Flichman, D., Scian, R., Rohr, C., Dopazo, H., Fernández Gianotti, T., ... Pirola, C. J. (2016). Mitochondrial genome architecture in non-alcoholic fatty liver disease. *The Journal of Pathology*. <https://doi.org/10.1002/path.4803> Sookoian, S., Rosselli, M. S., Gemma, C., Burgueño, A. L., Fernández Gianotti, T., Castaño, G. O., & Pirola, C. J. (2010). Epigenetic regulation of insulin resistance in nonalcoholic fatty liver disease: Impact of liver methylation of the peroxisome proliferator-activated receptor  $\alpha$  1 promoter. *Hepatology*, 52(6). <https://doi.org/10.1002/hep.23927>



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

**Manuscript NO:** 35987

**Title:** miR-192-5p regulates lipid synthesis in non-alcoholic fatty liver disease through SCD-1

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**Reviewer's country:** Spain

**Science editor:** Li Ma

**Date sent for review:** 2017-10-05

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**Review time:** 7 Hours

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

This paper was focused in determining the hepatic levels of miR-192-5p in NAFLD animal models in order to demonstrate its role on lipid accumulation. In general, the English is acceptable, but minor changes are needed. Further, some major changes still need to be addressed.

1. Introduction: - Please, change epigenetic alterations for epigenetic mechanisms - Authors must review abbreviations list, i.e. SD in the abstract

2. Material and methods: - Please, clarify how authors isolated microRNA profile and the specific quantification method employed. Due to the small size of these microRNAs, targeted methods should be required. - Please, justify the employ of the microRNA housekeeping genes. - Please, detail the experiments performed to isolate and purify microRNAs from Huh 7 cells

3. Results: - Please, when referring to NAFLD in animal models, clarify if its regarding to simple steatosis or NASH, due to this disease



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comprised two distinct entities. - Please, justify why after liraglutide injection, body weight decreased below control animals. - Please, in figure 1B clarify whether hepatic TG in liraglutide vs control model was found to be statistically lower. - Please, in figure 1D comparisons should be also performed among liraglutide and control animals, as well as in figure 1E, protein levels. - Please, change lipid drops by lipid droplets. - Please, add the reference in figure 2A, y-axis - Please, characterize the animal model, at least insert a table including biochemical and lipid panels, as well as liver evaluation.