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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 43124

Title: Exploratory metabolomics of metabolic syndrome: A status report

Reviewer's code: 03465354

Reviewer's country: United States

Science editor: Jia-Ping Yan

Date sent for review: 2018-11-19

Date reviewed: 2018-11-21

Review time: 2 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	[ ] Accept (High priority)	Peer-Review:
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Accept (General priority)	[Y] Anonymous
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Minor revision	[ ] Onymous
[ ] Grade D: Fair	[ ] Grade D: Rejection	[Y] Major revision	Peer-reviewer's expertise on the topic of the manuscript:
[ ] Grade E: Do not publish		[ ] Rejection	[ ] Advanced
			[Y] General
			[ ] No expertise
			Conflicts-of-Interest:
			[ ] Yes
			[Y] No

SPECIFIC COMMENTS TO AUTHORS

The proposed mini-review by Lent-Schochet et al. entitled "Exploratory metabolomics of metabolic syndrome: A status report" gives a snap-shot of the current knowledge of the role of various metabolites in the development, diagnosis and treatment of metabolic syndrome as well as of their potential to interfere with inflammatory signaling pathways.

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The review starts with an introduction section defining the pathophysiology of the metabolic syndrome and related pathological conditions, followed by sections for specific biogenic amines, amino acids, branched chain amino acids, and aromatic amines. Based on the provided information, the authors of the manuscript conclude that the analysis of particular metabolites may help to better characterize metabolic syndrome and its pathogenesis. This review follows straight logic and is written in a clear language. Main weakness of the present work in my opinion as a peer reviewer is the lack of specific details when previous studies are described. Information about what specific dose and time period of stimulation, way of administration, type of solvent used, concentrations in circulation, etc. is important to be provided when discussing supplementation with a specific agent. Also, when describing a change of particular analyte, the magnitude of change also needs to be given. Few examples of such lack of information include: p. 3 ("LC supplementation in humans…", "…positively correlated…", "…inversely to the important anti-inflammatory adipokine…"), p. 5 ("…glutamate levels were donw-regulated compared to controls"), p. 6 ("…supplementation of L-arginine…", "…L-arginine treatment improves…", "…decreases pro-inflammatory cytokines…"), p. 7 ("…histidine supplementation…", "…decreased inflammation and oxidative stress…"), etc. Minor comments: - p. 7, Histidine section, "…after bariatric surgery": Please be specific about the type of bariatric surgery. - p. 7, Methionine/Cysteine section, "Adams et al.": Is this the same reference # 44 (Adams as a single author) or a different reference? - p. 8, Lysine section: Reference for Ilda et al. (reference # 50) is missing in the text. Despite these limitations, in my opinion, this study is informative and it would be of interest to the scientists and clinicians working in the field.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 43124

Title: Exploratory metabolomics of metabolic syndrome: A status report

Reviewer's code: 00507108

Reviewer's country: Ireland

Science editor: Jia-Ping Yan

Date sent for review: 2018-11-19

Date reviewed: 2018-11-26

Review time: 7 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [Y] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This is an interesting review by Authors who have extensively published on the subject. The introduction to Biogenic amines reference only one review which clearly points out the uncertainty of the TMAO story. This would be better summarised. It is a 2016 article and allows the authors to detail advances in Knowledge since then. For example Ref 8

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which is wrongly reported shows that CRP IL6 and TNFa are lower in subjects whose level is more than 310mg/dl. This might be in keeping with the new studies which suggest that high fat diet might not be that bad in atherosclerotic terms.(PURS study for example. Ref 9 does not examine supplementation. The sentence ;Other studies have shown it has a role inCVD should be referenced critically. Since betaine is a metabolite of choline metabolism is it not a given that there an inverse relationship between Betaine and Choline? Insulin resistance in mice and choline deficient diet interesting Ref 10 2006 but what about Gao R et al nutrition 2017 showing that in humans a high choline diet is associated with insulin sensitivity? Would the article by Roe AJ et al 2017 Am J Clin Nutr and Svinger GF 2016 Clin Chem 2016 not be worth a mention? The section on amino acids might also benefit from some more up to date references. A suggestion Wang S et al Clin Chim Acta 2018 tHart lM J Clin Endocrinol Metab 2018 Paprott R et al J Diab Res 2018 Choi YS et al 2018 Metabolic Syndr rel disorders, Further articles worth considering Ganz T Diabetes Metabolism Res Rev 2017 Deveaux AJ J Nutr 2016 The conclusion is reasonable but perhaps more in the text about metabolomics and what they have so far shown would be helpful to support the conclusion. In conclusion a very interesting article but the reader is too often left with the idea that nothing much has changed in our knowledge in the last 10 years

INITIAL REVIEW OF THE MANUSCRIPT

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