



SDI Review Form 1.6

Journal Name:	International Journal of Biochemistry Research & Review
Manuscript Number:	Ms_IJBCRR_29575
Title of the Manuscript:	New insight on growth differentiation factor 15, interleukin 4 and fetuin A: linking role in diabetes mellitus type 2 with cardiovascular risk
Type of the Article	Original Research Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	1. The authors claim to highlight the role of a biomarker network in cardiovascular diabetic complications, "to better understanding of the pathogenesis of T2DM with CVD". For this purpose they analyse the changes in 6 bioparameters: plasminogen activator inhibitor-1 (PAI-1), fetuin A, interleukin-4 (IL-4), nitric oxide (NO), advanced oxidation protein products (AOPPs) and growth differentiation factor 15 (GDF-15). However, in the title only three of them were marked, i.e. GDF-15, IL-4, and fetuin A "as newly investigated biomarkers of T2DM complicated by CVD". 2. Because all the studied parameters were properly described (with literature data on mechanisms of action in the pathogenesis of T2DM and CVD); were included in the tables, where their levels were statistically compared to those of healthy controls, and between the two groups of T2DM patients, we believe that this should be reflected in the title (e.g. "Linking role of a biomarker network on type 2 diabetes mellitus with cardiovascular risk") or something. 3. With regard to evaluation of the diagnostic and "potential prognostic" role of GDF-15, IL-4 and fetuin A in T2DM with CVD, this can not be done	Our responses are presented below and we are looking forward and ready to respond to any future comment (s) 1- We totally agree on this point but the title will be very long if I put all parameters in the title, so I choose 3 of them which are not previously studied as a biomarker network in diabetes with CVD. However, I take in my consideration your valuable comment number 2 in redesigning the article title. 2-We totally agree on this point and we have rephrased it and highlighted in the main text by yellow 3- We totally agree on this point. But we are trying to discover new biomarkers that may be in the future



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	only by the larger increase (or decrease) of the values of these markers in the T2DM group with CVD compared to the group without CVD, because many different factors might play a role in the process. 4. The sample size is very small for the big tasks that the authors set themselves: diagnostic and predictive role of peak concentration of various inflammatory biomarkers in diabetics with CVD, as well as to clarify the pathogenesis of the disease. Therefore, it is well to note that the data in the article are preliminary and need confirmation, or as others said “it should be considered a hypothesis generator”. 5. The article is full of very long sentences, making it difficult to read and understand. 6. The discussion is overloaded by literature on mechanisms of action of the biomarkers and need to lighten up, focusing mainly to justify the thesis of the authors. 7. The comments do not deny all dignity of the article and it could be published after processing in the said directions.	as a part of multi-markers panel. And on our ongoing research we will take this point in our consideration and compare our biomarker network with others which are specific for CVD. 4- We totally agree on this point and we have reported this in the conclusion part (further researches with larger sample size are required for confirmation of our current study) 5- We rephrased long sentences again. 6- We reconstructed the discussion part again.
<u>Minor</u> REVISION comments		
<u>Optional/General</u> comments		