



Glimepiride Compared to Liraglutide Increases Plasma Levels of miR-206, miR-182-5p, and miR-766-3p in Type 2 Diabetes Mellitus: A Randomized Controlled Trial (*Diabetes Metab J* 2023;47:668-81)

Nikolai N. Scherbak^{1,*}, Robert Kruse^{2,3,*}, Thomas Nyström⁴, Johan Jendle⁵

¹Life Science Center, Örebro University, School of Science and Technology, Örebro,

²Department of Clinical Research Laboratory, ³Inflammatory Response and Infection Susceptibility Center (iRiSC), Faculty of Medicine and Health, Örebro University, Örebro,

⁴Karolinska Institutet, Department of Clinical Science and Education, Södersjukhuset, Stockholm,

⁵School of Medical Sciences, Faculty of Medicine and Health, Örebro University, Örebro, Sweden

We appreciate Dr. Lee's insightful comments regarding our recently published article, titled "Glimepiride compared to liraglutide increases plasma levels of miR-206, miR-182-5p, and miR-766-3p in type 2 diabetes mellitus: a randomized controlled trial [1]." The growing body of evidence suggests that microRNAs (miRNAs) play a significant role in the pathogenesis of type 2 diabetes mellitus (T2DM) [2,3]. Nevertheless, only a limited number of studies have explored variations in miRNA expression in response to glucose-lowering drugs [4].

It is crucial to recognize that the miRNAs identified in our study (miR-206, miR-182-5p, and miR-766-3p) have previously been proposed as biomarkers for various diseases apart from T2DM [5-9]. That is why it is essential to notice that the expression of these miRNAs is not solely specific to a particular disease but can also be influenced by medical treatments, such as glimepiride. Thus, investigations about the effect of glucose-lowering drugs on miRNAs' expression are of importance in our understanding of the molecular mechanisms underpinning the actions of these drugs and in shaping personalized treatment strategies.

It is also important to clarify that the aim of our study was not to suggest biomarkers and therefore did not have the de-

sign needed to generalize and validate findings outside of our study population [10]. As stated in the conclusion, we see a future need to evaluate miRNAs as potential biomarkers, or bio-signatures. In relation to our findings, we see a need for further research to evaluate miR-206, miR-182-5p, and miR-766-3p in the context of diagnosis, prognosis and therapy response of T2DM.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Scherbak NN, Kruse R, Nystrom T, Jendle J. Glimepiride compared to liraglutide increases plasma levels of miR-206, miR-182-5p, and miR-766-3p in type 2 diabetes mellitus: a randomized controlled trial. *Diabetes Metab J* 2023;47:668-81.
2. Barbagallo D, Piro S, Condorelli AG, Mascali LG, Urbano F, Parrinello N, et al. miR-296-3p, miR-298-5p and their downstream networks are causally involved in the higher resistance

Corresponding author: Johan Jendle <https://orcid.org/0000-0003-1025-1682>
School of Medical Sciences, Faculty of Medicine and Health, Örebro University,
SE-70182 Örebro, Sweden
E-mail: johan.jendle@oru.se

*Nikolai N. Scherbak and Robert Kruse contributed equally to this study as first authors.

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- of mammalian pancreatic α cells to cytokine-induced apoptosis as compared to β cells. *BMC Genomics* 2013;14:62.
3. Guay C, Regazzi R. New emerging tasks for microRNAs in the control of β -cell activities. *Biochim Biophys Acta* 2016;1861(12 Pt B):2121-9.
 4. Demirsoy IH, Ertural DY, Balci S, Cinkir U, Sezer K, Tamer L, et al. Profiles of circulating miRNAs following metformin treatment in patients with type 2 diabetes. *J Med Biochem* 2018;37: 499-506.
 5. Li X, Li Y, Zhao L, Zhang D, Yao X, Zhang H, et al. Circulating muscle-specific miRNAs in Duchenne muscular dystrophy patients. *Mol Ther Nucleic Acids* 2014;3:e177.
 6. Toivonen JM, Manzano R, Olivan S, Zaragoza P, Garcia-Re-dondo A, Osta R. MicroRNA-206: a potential circulating bio-marker candidate for amyotrophic lateral sclerosis. *PLoS One* 2014;9:e89065.
 7. Liu X, Zheng W, Zhang X, Dong M, Sun G. The diagnostic and prognostic value of serum miR-206 in colorectal cancer. *Int J Clin Exp Pathol* 2017;10:7528-33.
 8. Jin P, Gu W, Lai Y, Zheng W, Zhou Q, Wu X. The circulating mi-croRNA-206 level predicts the severity of pulmonary hyperten-sion in patients with left heart diseases. *Cell Physiol Biochem* 2017;41:2150-60.
 9. Zhu L, Chen T, Ye W, Wang JY, Zhou JP, Li ZY, et al. Circulating miR-182-5p and miR-5187-5p as biomarkers for the diagnosis of unprotected left main coronary artery disease. *J Thorac Dis* 2019;11:1799-808.
 10. FDA Center for Drug Evaluation and Research. Biomarker qualification: evidentiary framework (FDA-2018-D-4267). Available from: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/biomarker-qualification-evidentiary-framework> (cited 2023 Oct 12).