British Journal of Multidisciplinary and Advanced Studies:
Chemistry and Biochemistry, *5(2),1-11, 2024*
Print ISSN: 2517-276X
Online ISSN: 2517-2778
https://bjmas.org/index.php/bjmas/index
Published by the European Centre for Research Training and Development UK

Identification of Three Novel Lipid Metabolism-Related Long Non-Coding RNAS (*GHRLOS*, *Lnc-GHRL-3:3*, and *LINC00852*) As Potential Biomarkers and Regulators for Diabetic Dyslipidemia

Dalia M. Anbari and Rowyda N. Al-Harithy*
Department of Biochemistry, King AbdulAziz University, Jeddah, Saudi Arabi

doi: https://doi.org/10.37745/bjmas.2022.0468 Published April 20, 2024

Citation: Anbari D.M. and Al-Harithy R.N. (2024) Identification of Three Novel Lipid Metabolism-Related Long Non-Coding RNAS (GHRLOS, Lnc-GHRL-3:3, and LINC00852) As Potential Biomarkers and Regulators for Diabetic Dyslipidemia, *British Journal of Multidisciplinary and Advanced Studies*: Chemistry and Biochemistry, 5(2),1-11

ABSTRACT: *Type 2 diabetes mellitus (T2DM) is a metabolic disease that affects both young and old people. The prevalence of T2DM is increasing worldwide and is reaching epidemic proportions. It is associated with a dysregulation of lipid metabolism that favors the development and progression of many diseases, including diabetic dyslipidemia. Therefore, in-depth studies are needed to understand the epigenetic mechanisms of diabetic dyslipidemia, especially at the molecular level. However, the underlying mechanisms are still largely unknown. In the current investigation, we aimed to elucidate novel potential lipid metabolism-related long non-coding RNAs (lncRNAs) that regulate diabetic dyslipidemia development and provide novel signatures for its prognosis and precise treatment. HbA1c levels and lipid profiles were analyzed in 71 T2DM patients and 32 non-diabetic controls using established assays. The expression patterns of the genes GHRLOS, lnc-GHRL-3:3, and LINC00852 were detected by quantitative real-time polymerase chain reaction (qRT-PCR).The results showed that the expression levels of the lncRNAs GHRLOS, lnc-GHRL-3:3, and LINC00852 were significantly ($P < 0.0001$) higher in diabetics compared to non-diabetics. Pearson's correlation analysis showed that the expression levels of GHRLOS, lnc-GHRL-3:3, and LINC00852 were significantly and negatively correlated with HbA1c, TC, TG, LDL, and VLDL and positively correlated with HDL. The results of the linear regression analysis confirmed the correlation in the same direction and the significance value of Pearson coloration coefficient analysis. Finally, it can be concluded that the lncRNAs GHRLOS, lnc-GHRL-3:3, and LINC00852 show a significant correlation with dyslipidemia in T2DM patients, indicating their potential roles as biomarkers and regulators of diabetic dyslipidemia.*
KEY WORDS: *GHRLOS*, lnc-*GHRL-3:3, LINC00852,* Lipid profile, Type 2 Diabetes Mellitus

British Journal of Multidisciplinary and Advanced Studies:
Chemistry and Biochemistry, *5(2),1-11, 2024*
Print ISSN: 2517-276X
Online ISSN: 2517-2778
https://bjmas.org/index.php/bjmas/index
Published by the European Centre for Research Training and Development UK

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major health burden worldwide and one of the most important modifiable cardiovascular diseases (CVD) risk factors (Goyal et al., 2023). It is well known that diabetic patients often present with atypical dyslipidemia, characterized by elevated triglycerides, low-high density lipoprotein cholesterol (HDL-C), and predominance of small-dense low-density lipoprotein (LDL) particles. People with dyslipidemia are twofold increased risk of CVD as compared to those with normal lipid levels (Mozaffarian et al. 2016; Ballard-Hernandez et al., 2023). Therefore, dyslipidemia is considered the major independent predictor of CVD in T2DM patients, which results in the high mortality and morbidity of diabetic patients (Chen et al., 2018; Kaze et al., 2021). Diabetic dyslipidemia is an important modifiable risk factor for CVD. Therefore, exploring the underlying regulatory mechanisms of lipid metabolism and signaling, and targeting the critical regulatory molecules will be beneficial for chronic disease treatment. Research fields have continued to improve, leading to a clearer comprehension of the intricate mechanisms controlling lipid metabolism. Technological advances in the human genome have shown that non-coding RNAs (ncRNAs) can function as a novel class of regulators in lipid metabolism (Zeng et al.,2018; Zhang et al., 2019; Zhang et al.,2020; Zhao et al., 2021).

Long non-coding RNAs (lncRNAs), a subclass of these ncRNAs, have become a focus of research because of the wide range of biological processes they perform (Zhang et al., 2019; Panni et al., 2020; Saw et al., 2021; Statello et al., 2021; Duan et al., 2023). Lately, it has become more widely recognized the role of diverse lncRNAs as critical regulatory players during the lipid metabolism process and lipid signaling (van Solingen et al., 2018). The intake, production, storage, and breakdown of lipids have all been identified to include these molecules (Chen et al., 2022; Zhang et al., 2019). Different strategies are used to carry out the lncRNAs regulatory function in lipid metabolism. They modify gene expression programs that are essential for preserving lipid balance in cells and tissues through their interactions with proteins, DNA, and other RNA molecules (Singh et al., 2018; Ulitsky., 2018; Statello et al., 2021). They can act as scaffolds, enhancer, bringing together diverse proteins involved in lipid metabolism and facilitating their functional interactions (Lu et al., 2021). Additionally, lncRNAs expression can be repressed by small RNAs, and lncRNAs can affect small RNA activity and abundance through competition for binding or by triggering small RNA degradation (Duan et al., 2023).

Identifying lncRNAs associated with diabetic dyslipidemia is a great challenge. Emerging evidence suggests that targeting specific lncRNAs may hold therapeutic potential for the treatment of lipid-related disorders and may provide a novel avenue for intervention. Therefore, the aim of this study is to evaluate the association between the lipid profile in individuals with T2DM and the expression levels of *GHRLOS*, *lnc-GHRL-3:3*, and *LINC00852*, which may indicate their function in diabetic dyslipidemia.

British Journal of Multidisciplinary and Advanced Studies:
Chemistry and Biochemistry, *5(2),1-11, 2024*
Print ISSN: 2517-276X
Online ISSN: 2517-2778
https://bjmas.org/index.php/bjmas/index
Published by the European Centre for Research Training and Development UK

MATERIALS AND METHODS

Patients and healthy individuals

National Committee of Biology and Medicine Ethics at King Abdul-Aziz University and Medical College, Jeddah, Saudi Arabia granted its clearance for this study (reference number: HA-02-J-008). The Diabetic and Endocrine Care Center in Jeddah, Saudi Arabia, provided 103 participants (71 T2DM patients and 32 non-diabetic controls) for the study. Participants had to be older than 40 and from Saudi Arabia. All subjects gave their informed consent prior to having their blood drawn. All T2DM patients had received their diagnosis for the condition for at least two years. They were all using insulin, metformin, or a combination of the two to treat their diabetes. The study did not include any T2DM patients who had other chronic conditions, such as cancer, heart disease, or renal failure, or who were on any other drugs. The non-diabetic subjects had HbA1c readings between 4.8% and 5.6%, were in good health, and were not receiving any medical treatment.

Blood collection and serum preparation

All participants had their venous blood samples drawn in plain tubes. In a refrigerated centrifuge (4°C), blood samples were centrifuged at 1,000–2,000 x g for 10 min after being kept undisturbed at room temperature for 15 min. The serum was transferred into sterilized tubes and stored at -20°C.

Anthropometric and biochemical measurements

All contributors' height, weight, and complete histories were gathered prior to sample collection. All participants had biochemical testing to determine their levels of fasting blood glucose (FBG), hemoglobin A1C (HbA1c), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and high-density lipoprotein (HDL). Using a Beckman Synchron CX9 analyzer, the enzymatic glucose oxidase technique was used to quantify FBG levels. Dimension EXL with an LM integrated clinical chemistry and immunoassay analyzer (Siemens Ltd, England) and D-10 Instrumentation (Bio-Rad, USA) was used to measure HbA1c. A VITROS Biochemistry Analyzer (KODAK, CA, USA) was used to examine the levels of serum TC, TG, and HDL. To compute LDL, the Friedewald formula [LDL= TC-(TG/5+HDL-C)] was used. The TG value was divided by 5 to determine the VLDL level in mg/dl.

Statistical analyses

Microsoft Excel and the GraphPad Prism version 8.0.2 program (GraphPad Software, La Jolla, California, USA) were used to conduct the statistical analyses. To compare the different variables between the two groups, Mann-Whitney U tests were used to compare the distinct variables between the two groups. The association of lncRNAs-*GHRL* expression levels with HbA1c and lipid profile was assessed using linear regression analysis and Pearson′s correlation coefficient.

Statistical significance was set at $P \leq 0.05$.

RESULTS

Physical and clinical characteristics of participants

A total of 103 participants (71 T2DM patients and 32 non-diabetic controls) made up the final sample. There were no significant differences between the diabetic and the non-diabetic controls regarding BMI, gender, and age. The levels of FBG, HbA1c, TC, TG, HDL, LDL, and VLDL between diabetic and non-diabetic controls were significantly different ($P < 0.001$) (Table 1).

Expression levels of *GHRLOS, lnc-GHRL-3:3,* and *LINC00852*

The findings demonstrated that diabetic participants expressed *GHRLOS, lnc-GHRL-3:3,* and *LINC00852* at different levels. They were significantly higher ($P < 0.0001$) than non-diabetic individuals (Table 2).

Correlation of *GHRLOS, lnc-GHRL-3:3,* and *LINC00852* expression levels with HBA1c and lipid profile

Using relative gene expression data, Pearson's correlation analysis showed that expression level of *GHRLOS, lnc-GHRL-3:3,* and *LINC00852* correlate significantly and negatively with HbA1c, TC, TG, LDL, and VLDL and positively with HDL (Table 3,4, and 5). The results of the linear regression analysis confirmed the association in the same direction and significance value of Pearson coloration coefficient analysis. The findings of the linear regression analysis corroborated the conclusions (Figures 1, 2, and 3).

DISCUSSION

Researchers have realized that lipid metabolism is not a self-regulating network because of ongoing study advancements. Extensive study has been conducted on distinct families of lncRNAs to understand the complex roles they play in lipid homeostasis. Emerging studies have demonstrated that lncRNAs can act as a novel class of regulators in the metabolism of lipids. Thus, we anticipate that finding new lncRNAs associated with diabetic dyslipidemia will help with the development of the condition and its accurate management. Thus, it is of great urgency to examine the prevalence of dyslipidemia in T2DM from an epigenetic standpoint. Determining the epigenetic variables associated with diabetic dyslipidemia is important for comprehending the underlying molecular processes and the origins of the condition development. Therefore, the molecular pathways underlying the development of diabetic dyslipidemia will provide a wealth of research opportunities for many years to come.

Although research into dyslipidemia is ongoing and developing, the role of lncRNAs *GHRLOS*, *lnc-GHRL-3:3*, and *LINC00852* in diabetic dyslipidemia remains unknown. Thus, investigations on this subject makes it especially important and necessary. In the present study, lncRNAs *GHRLOS*, *lnc-GHRL-3:3*, and *LINC00852* were identified as novel biomarkers for diabetic dyslipidemia. According to our research, in individuals with diabetes, the expression levels of *GHRLOS*, *lnc-GHRL-3:3*, and *LINC00852* were significantly ($P < 0.0001$) higher in diabetics compared to non-diabetics. Pearson's correlation analysis showed that the expression levels of *GHRLOS*, *lnc-GHRL-3:3*, and *LINC00852* were significantly and negatively correlated with HbA1c, TC, TG, LDL, and VLDL and positively correlated with HDL. The results of the linear regression analysis confirmed the correlation in the same direction and the significance value of Pearson coloration coefficient analysis.

GHRLOS gene is an antisense to the ghrelin (*GHRL*) gene. In human, it is located on chromosome 3p25.3 which alternatively spliced into multiple isoforms. *GHRLOS* lncRNA was first discovered by Seim and his colleagues (Seim et al.,2007)). They reported that *GHRLOS* RNA gene completely overlaps the *GHRL* gene and spans the promoter and untranslated regions of the *GHRL* gene. A year later, the same group published an article about the complex organization of *GHRLOS* RNA gene. They showed that the *GHRLOS* RNA gene exhibits feature which are common to many non-coding RNA genes, including extensive splicing, lack of significant and conserved open reading frames, and differential expression. Their data also reveal that *GHRLOS* contains multiple first exons and that it overlaps both *GHRL* gene and a novel SEC13 exon in the antisense direction, suggesting that *GHRLOS* may have a role in regulating of *GHRL* gene and SEC13 exon (Seim et al., 2008). Among the three lncRNA signatures identified in this investigation is *lnc-GHRL-3:3*. The gene *lnc-GHRL-3:3* is a sense intronic with a length of 295bp and located within ghrelin gene in chromosome 3 (chr3:10290828-10291120). Recently, *lnc-GHRL-3:3* was identified as a novel lncRNA biomarker that might be involved in the regulation mechanisms of T2DM and may be used as potential biomarkers of T2DM (Anbari et al., 2023). The third signature found in this investigation is the long intergenic non-coding RNA 00852 (*LINC00852)*, is a sense intronic ncRNA gene located on chromosome 3 (chr3:10284419-10285746). The gene *LINC00852* was first discovered in lung adenocarcinoma. The investigators showed that *LINC00852* is overexpressed in lung adenocarcinoma spinal metastasis tissues and functions as an oncogene by promoting the proliferation, migration, and invasion of lung adenocarcinoma cells (Liu et al., 2018). Further work showed that overexpression of *LINC00852* could promote the proliferation and metastasis of prostate cancer cells (Yi et al., 2021) and ovarian cancer cells (Qiao et al., 2021). It's worth noting that *LINC00852* was found to be associated with poor prognosis in non-small cell lung cancer (NSCLC) patients. Tuo and his team sproposed *LINC00852* as an NSCLC predictive biomarker. They also implied that the epigenetic signaling pathway of LINC00852/has-miR-145-5p/KLF may be considered as a novel molecular target for fighting NSCLC (Tuo et al., 2021). The gene *LINC000852* was recently identified as a novel and promising biomarker for early

detection of T2DM. The investigators suggested that *LINC000852* might have a regulatory role in the development of T2DM (Al-Harithy et al., 2020).

To date, there is a significant difference between the number of lncRNAs being discovered and those that have comprehensive functional descriptions. This is due, in part, to the variety and complexity of the processes through which lncRNAs work as well as the current absence of prediction methods that could expedite the functional characterization of lncRNAs. A current challenge is to translate the observed changes in expression and localization of lncRNAs to the discovery of their functions.

Research in the field documented over 60 lncRNAs, including *SRA*, *HULC*, *lncLSTR*, *APOA1-AS*, *MEG3*, *H19*, *AT115872*, *AT102202* and *lincRNA-DYNLRB2–2*, can regulate lipid metabolism by a variety of direct or indirect mechanisms (Zhang et al., 2020). Liu and his team found that the lncRNA *AT115872* can act from a distance on the expression of genes that encode pivotal enzymes for cholesterol absorption. Conversely, they found that the lncRNA *AT102202* can act locally on genes that encode vital enzymes in cholesterol anabolism (Liu et al., 2015). Sallam and his co-workers found that lncRNA *LeXis* contribute to the downregulation of genes involved in the biosynthesis of cholesterol and HDL (Sallam et al., 2016). Li and his team reported that the lncRNA *LASER* is a key player in the regulation of cholesterol metabolism via HNF-1α and *PCSK9* (Li et al., 2019). A year later, Liu and his group revealed that the lncRNA *MALAT1* simulate the accumulation of cholesterol through the action on the miR-17-5p/ABCA1 axis (Liu et al., 2020).

As far as we are aware, lipid metabolism-related lncRNAs have been regarded as potential therapeutic targets for multiple disease treatments (Lu et al., 2021; Wang et al., 2022; Tan et al., 2023). Further investigations into the functions and mechanisms of lncRNAs in lipid metabolism are warranted, with the potential to uncover new therapeutic targets and strategies for addressing lipid-related disorders. Therefore, targeting *GHRLOS*, *lnc-GHRL-3:3*, and *LINC00852* may provide novel strategies for reducing lipid metabolism-related diseases risk. Our current knowledge of lncRNAs in lipid metabolism is just the tip of the iceberg. The rest of the iceberg is waiting to be explored.

CONCLUSION

Our study indicates that lncRNAs *GHRLOS, lnc-GHRL-3:3,* and *LINC00852* are potentially causal for lipid profile variations, and they might play a role in the regulation of lipid metabolism in patients with T2DM. Thus, to locate potential biomarkers relevant to the phenotype of diabetic dyslipidemia, lncRNAs *GHRLOS, lnc-GHRL-3:3,* and *LINC00852* are the suggestion.

Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Goyal R, Singhal M, Jialal I. (2023) Type 2 Diabetes. 2023 Jun 23. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
2. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. (2016) Heart disease and stroke statistics—2016 update: A report from the American Heart Association. Circulation. 133(4), e38–60.
3. Ballard-Hernandez J, Sall J. (2023) Dyslipidemia Update. Nurs Clin North Am. 58(3), 295-308.
4. Chen C, Cui Q, Zhang X, Luo X, Liu Y, Zuo J, Peng Y. (2018) Long non-coding RNAs regulation in adipogenesis and lipid metabolism: Emerging insights in obesity. Cell Signal. 51,47-58.
5. Kaze AD, Santhanam P, Musani SK, Ahima R, Echouffo-Tcheugui JB. (2021) Metabolic Dyslipidemia and Cardiovascular Outcomes in Type 2 Diabetes Mellitus: Findings From the Look AHEAD Study. J Am Heart Assoc. 10(7), e016947.
6. Zeng Y, Ren K, Zhu X, Zheng Z, Yi G. (2018) Long Noncoding RNAs: Advances in Lipid Metabolism. Adv Clin Chem. 87,1-36.
7. Zhang X, Price NL, Fernández-Hernando C. (2019) Non-coding RNAs in lipid metabolism. Vascul Pharmacol. 114,93-102.
8. Zhang TN, Wang W, Yang N, Huang XM, Liu CF. (2020) Regulation of Glucose and Lipid Metabolism by Long Non-coding RNAs: Facts and Research Progress. Front Endocrinol (Lausanne).11,457.
9. Zhao X, Zeng H, Lei L, Tong X, Yang L, Yang Y, et al. (2021) Tight junctions and their regulation by non-coding RNAs. Int J Biol Sci. 17(3),712-727.
10. Zhang P, Wu W, Chen Q, Chen M. (2019) Non-Coding RNAs and their Integrated Networks. J Integr Bioinform.16(3),20190027.
11. Panni S, Lovering RC, Porras P, Orchard S. (2020) Non-coding RNA regulatory networks. Biochim Biophys Acta Gene Regul Mech.1863(6),194417.
12. Saw PE, Xu X, Chen J, Song EW. (2021) Non-coding RNAs: the new central dogma of cancer biology. Sci China Life Sci. 64(1),22-50.
13. Statello L, Guo CJ, Chen LL, Huarte M. (2021) Gene regulation by long non-coding RNAs and its biological functions. Nat Rev Mol Cell Biol. 22(2),96-118.
14. Duan J, Huang Z, Nice EC, Xie N, Chen M, Huang C. (2023) Current advancements and future perspectives of long noncoding RNAs in lipid metabolism and signaling. J Adv Res. 48,105-123.
15. van Solingen C, Scacalossi KR, Moore KJ. (2018) Long noncoding RNAs in lipid metabolism. Curr Opin Lipidol. 29(3),224-232.

16. Chen E, Yi J, Jiang J, Zou Z, Mo Y, Ren Q, et al. (2022) Identification and validation of a fatty acid metabolism-related lncRNA signature as a predictor for prognosis and immunotherapy in patients with liver cancer. BMC Cancer. 22(1),1037.
17. Zhang X, Wang W, Zhu W, Dong J, Cheng Y, Yin Z, et al. (2019) Mechanisms and Functions of Long Non-Coding RNAs at Multiple Regulatory Levels. Int J Mol Sci. 20(22),5573.
18. Singh AK, Aryal B, Zhang X, Fan Y, Price NL, Suárez Y, et al. (2018) Posttranscriptional regulation of lipid metabolism by non-coding RNAs and RNA binding proteins. Semin Cell Dev Biol. 81,129-140.
19. Ulitsky I. (2018) Interactions between short and long noncoding RNAs. FEBS Lett. 592(17),2874-2883.
20. Lu Q, Guo P, Liu A, Ares I, Martínez-Larrañaga MR, Wang X, et al. (2021) The role of long noncoding RNA in lipid, cholesterol, and glucose metabolism and treatment of obesity syndrome. Med Res Rev. 41(3),1751-1774.
21. Duan J, Huang Z, Nice EC, Xie N, Chen M, Huang C. (2023) Current advancements and future perspectives of long noncoding RNAs in lipid metabolism and signaling. J Adv Res. 48,105-123.
22. Seim I, Collet C, Herington AC, Chopin LK. (2007) Revised genomic structure of the human ghrelin gene and identification of novel exons, alternative splice variants and natural antisense transcripts. BMC Genomics. 8,298.
23. Seim I, Carter SL, Herington AC, Chopin LK. (2008) Complex organisation and structure of the ghrelin antisense strand gene GHRLOS, a candidate non-coding RNA gene. *BMC* Mol Biol. 9,95.
24. Anbari DM, Al-Harithy RN. (2023) Ghrelin intronic lncRNAs, *lnc-GHRL-3:2* and *lnc-GHRL-3:3*, as novel biomarkers in type 2 diabetes mellitus. Arch Physiol Biochem. 129(1),241-245.
25. Liu P, Wang H, Liang Y, Hu A, Xing R, Jiang L, et al. (2018) LINC00852 Promotes Lung Adenocarcinoma Spinal Metastasis by Targeting S100A9. J Cancer. 9(22),4139-4149.
26. Yi S, Li G, Sun B. (2021) Overexpression of LINC00852 promotes prostate cancer cell proliferation and metastasis. Asia Pac J Clin Oncol.17(6),435-44.
27. Qiao ZW, Jiang Y, Wang L, Wang L, Jiang J, Zhang JR, et al. (2021) LINC00852 promotes the proliferation and invasion of ovarian cancer cells by competitively binding with miR-140-3p to regulate AGTR1 expression. BMC Cancer. 21(1),1004.
28. Tuo Z, Liang L, Zhou R. (2021) LINC00852 is associated with poor prognosis in non-small cell lung cancer patients and its inhibition suppresses cancer cell proliferation and chemoresistance via the hsa-miR-145-5p/KLF4 axis. J Gene Med. 23(12), e3384.
29. Al-Harithy R, Anbari D. (2020) Downregulation of Circulating Long Non-Coding RNAs *GHRLOS* and *LINC00852* Associated with Type 2 Diabetes Mellitus. J Dis Markers. 5(1),1038.

30. Zhang TN, Wang W, Yang N, Huang XM, Liu CF. (2020) Regulation of Glucose and Lipid Metabolism by Long Non-coding RNAs: Facts and Research Progress. Front Endocrinol (Lausanne). 11,457.
31. Liu G, Zheng X, Xu Y, Lu J, Chen J, Huang X. (2015) Long non-coding RNAs expression profile in HepG2 cells reveals the potential role of long non-coding RNAs in the cholesterol metabolism. Chin Med J (Engl).128(1),91-7.
32. Sallam T, Jones MC, Gilliland T, Zhang L, Wu X, Eskin A, et al. (2016) Feedback modulation of cholesterol metabolism by the lipid-responsive non-coding RNA LeXis. Nature. 534(7605),124-8.
33. Li C, Hu Z, Zhang W, Yu J, Yang Y, Xu Z, et al. (2019) Regulation of Cholesterol Homeostasis by a Novel Long Non-coding RNA LASER. Sci Rep. 9(1):7693.
34. Liu L, Tan L, Yao J, Yang L. (2020) Long non-coding RNA MALAT1 regulates cholesterol accumulation in ox-LDL-induced macrophages via the microRNA-17-5p/ABCA1 axis. Mol Med Rep. 21(4):1761-1770.
35. Lu Q, Guo P, Liu A, Ares I, Martínez-Larrañaga MR, Wang X, et al. (2021) The role of long noncoding RNA in lipid, cholesterol, and glucose metabolism and treatment of obesity syndrome. Med Res Rev.41(3),1751-1774.
36. Wang Y, Li Q, Wang S, Wang BJ, Jin Y, Hu H, et al. (2022) The role of noncoding RNAs in cancer lipid metabolism. Front Oncol.12,1026257.
37. Tan Z, Fu S, Zuo J, Wang J, Wang H. (2023) Prognosis analysis and validation of lipid metabolism-associated lncRNAs and tumor immune microenvironment in bladder cancer. Aging (Albany NY).15(16),8384-8407.

British Journal of Multidisciplinary and Advanced Studies:
Chemistry and Biochemistry, *5(2),1-11, 2024*
Print ISSN: 2517-276X
Online ISSN: 2517-2778
https://bjmas.org/index.php/bjmas/index
Published by the European Centre for Research Training and Development UK

Table 1: Demographic and clinical characteristics of the study subjects

Parameters	Diabetic (n = 71) Mean ± SD	Non-diabetic (n = 32) Mean ± SD	*P-value*
Age (years)	57. 5 ± 9. 5	45. 5 ± 6. 5	0.51
Gender (M/F) %	36 (50.7) % / 35 (49. 29%)	17(53.12%) / 15 (46. 88%)	0.4
Duration of disease (years)	13.056 ± 5.72	-	-
BMI (kg/m^2)	31.69 ± 5. 33	28. 91 ± 4. 20	0.28
FBG (mmol/L)	8.51 ± 1.61	5.30 ± 0.31	0.0001***
HbA1c (%)	8. 09 ± 1.53	5. 31 ± 0. 30	0.001**
Total cholesterol (TC) (mg/dl)	175.77 ± 41.31	138 ± 20	0.0001***
Triglyceride (TG) (mg/dl)	148.85 ± 62.21	100.21 ± 16.89	0.0001***
HDL-c (mg/dl)	41.36 ± 12.03	48.28 ± 5.81	0.0001***
LDL-c (mg/dl)	111.28 ± 38.17	76.70 ± 14.91	0.0001***
VLDL-c (mg/dl)	29.77 ± 12.44	20.04 ± 3.37	0.0001***

Data are presented as means ± standard deviation, number (%) or median. M/F, male/female; BMI, body mass index; FBG, fasting blood glucose; HbA1c, hemoglobin A1c; TC, total cholesterol; TG, triglyceride; HDL-c, high density lipoprotein-cholesterol; LDL-c, low density lipoprotein-cholesterol; VLDL-c, very low-density lipoprotein-cholesterol; statistical analysis, Mann-Whitney U test.

Table 2: Relative expression values of *GHRLOS*, *lnc-GHRL-3:3,* and LINC00852

Gene	Diabetic (n=71) (ΔCt ± SD)	Non-diabetic (n=32) (ΔCt ± SD)	*P*-value
GHRLOS	8.9 ± 1.3	6.04 ± 0.9	<0.0001****
Lnc-GHRL-3:3	8.92 ± 1.72	5.50 ± 1.51	<0.0001****
LINC00852	9.7 ± 1.8	6.4 ± 1.2	<0.0001****

Table 3: Pearson correlation between *GHRLOS* expression with HbA1c and lipid profile

Parameters	R	*P* value
HbA1c (%)	-0.50	< 0.0001****
TC (mg/dl)	-0.30	0.002**
TG (mg/dl)	-0.19	0.05*
HDL-c (mg/dl)	0.20	0.05*
LDL-c (mg/dl)	-0.37	0.0002***
VLDL-c (mg/dl)	-0.2	0.05*

Table 4: Pearson correlation between *lnc-GHRL-3:3* expression with HbA1c and lipid profile

Parameters	R	*P* value
HbA1c (%)	-0.49	< 0.0001****
TC (mg/dl)	-0.40	< 0.0001****
TG (mg/dl)	-0.35	0.0003***
HDL-c (mg/dl)	0.35	0.0004***
LDL-c (mg/dl)	-0.47	< 0.0001****
VLDL-c (mg/dl)	-0.35	0.0003***

British Journal of Multidisciplinary and Advanced Studies:
Chemistry and Biochemistry, *5(2),1-11, 2024*
Print ISSN: 2517-276X
Online ISSN: 2517-2778
https://bjmas.org/index.php/bjmas/index
Published by the European Centre for Research Training and Development UK

Table 5: Pearson correlation between *LINC00852*

Parameters	R	*P* value
HbA1c (%)	-0.46	<0.0001****
TC (mg/dl)	-0.33	0.0006***
TG (mg/dl)	-0.19	0.05*
HDL-c (mg/dl)	0.24	0.01*
LDL-c (mg/dl)	-0.37	0.0002***
VLDL-c (mg/dl)	-0.19	0.05*

HbA1c, glycated hemoglobin; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; VLDL, very-low-density lipoprotein cholesterol

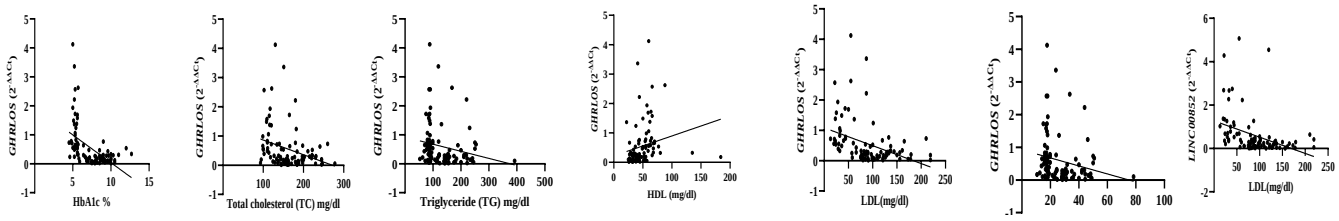

Figure 1: Linear regression analysis between *GHRLOS* expression level with HbA1c, TC, TG, HDL, LDL, and VLDL.

Figure 2: Linear regression analysis between *lnc-GHRL-3:3* expression level with HbA1c, TC, TG, HDL, LDL, and VLDL.

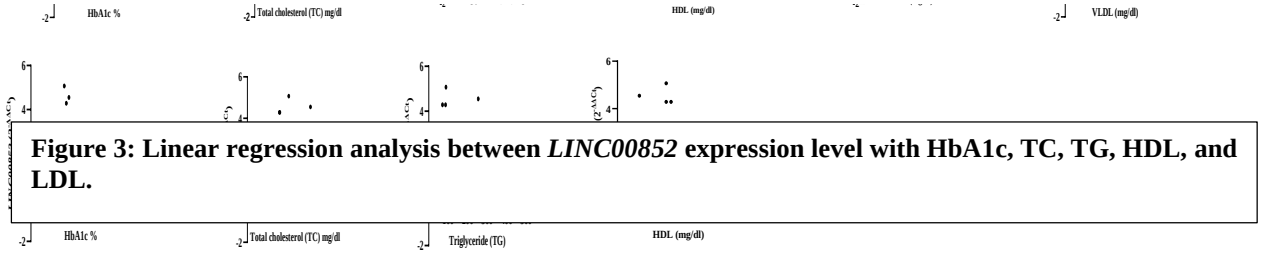

Figure 3: Linear regression analysis between *LINC00852* expression level with HbA1c, TC, TG, HDL, and LDL.