High-Density Lipoprotein Cholesterol and Nuclear Factor I A in Type 2 Diabetes and Mild Cognitive Impairment: biomarkers and mechanistic insights

Keywords
HDL-C, NHANES, Type 2 diabetes, Mendelian randomization, Mild cognitive impairment

Abstract

Introduction

Type 2 diabetes (T2D) and mild cognitive impairment (MCI) are interrelated conditions that significantly impair quality of life. This study aimed to identify a feasible biomarker for assessing T2D-MCI risk and to evaluate a potential therapeutic strategy.

Material and methods

We integrated data from the National Health and Nutrition Examination Survey (NHANES) with Mendelian randomization (MR) to investigate genetic causal relationships between T2D, MCI, and their shared biomarkers. Transcriptomic analysis identified T2D-associated genes. Clinical trials evaluated the short-term effects of modified fasting therapy (MFT) on glucose regulation and cognitive function. Cellular assays and patient samples validated key genes' roles in biochemical markers and downstream pathways.

Results

Among 6,356 T2D and 1,138 MCI subjects, vitamin D, high-density lipoprotein cholesterol (HDL-C), globulin, and creatinine were associated with both conditions. MR analysis showed that higher HDL-C levels reduced T2D risk (0.9059, 95% CI: 0.8666–0.9470) but increased MCI risk (OR = 1.0482, 95% CI: 1.0216–1.0755). Nuclear Factor I A (NFIA) was identified as a key HDL-C regulator. In a clinical cohort (17 T2D patients and 23 controls), MFT reduced body mass index fasting glucose, and HDL-C, increased NFIA expression, and improved Montreal Cognitive Assessment scores, especially in T2D-MCI patients. HDL-C rebounded at six months. In vitro, NFIA overexpression increased intracellular HDL-C and suppressed NF-κB signaling, while NFIA knockdown reduced APOA1 and APOE.

Conclusions

HDL-C has divergent genetic effects on T2D and MCI. NFIA modulates HDL-C and NF-κB activity, supporting metabolic and cognitive improvements. Targeting NFIA through MFT may represent a promising strategy for T2D-MCI prevention and treatment.

High-Density Lipoprotein Cholesterol and Nuclear Factor I A in Type 2 Diabetes and Mild Cognitive Impairment: biomarkers and mechanistic insights

Running title: HDL-C and *NFIA* in T2D and MCI

Abstract:

Introduction: Type 2 diabetes (T2D) and mild cognitive impairment (MCI) are interrelated conditions that significantly impair quality of life. This study aimed to identify a feasible biomarker for assessing T2D-MCI risk and to evaluate a potential therapeutic strategy.

Materials and methods: We integrated data from the National Health and Nutrition Examination Survey (NHANES) with Mendelian randomization (MR) to investigate genetic causal relationships between T2D, MCI, and their shared biomarkers. Transcriptomic analysis identified T2D-associated genes. Clinical trials evaluated the short-term effects of modified fasting therapy (MFT) on glucose regulation and cognitive function. Cellular assays and patient samples were used to validate the regulatory roles of key genes in biochemical markers and downstream signaling pathways.

Results: Among 6,356 T2D and 1,138 MCI subjects, vitamin D, high-density lipoprotein cholesterol (HDL-C), globulin, and creatinine were associated with both conditions. MR analysis showed that higher HDL-C levels reduced T2D risk (0.9059, 95% CI: 0.8666–0.9470) but increased MCI risk (OR = 1.0482, 95% CI: 1.0216–1.0755). Nuclear Factor I A (*NFIA*) was identified as a key HDL-C regulator. In a clinical cohort (17 T2D patients and 23 controls), MFT reduced body mass index fasting glucose, and HDL-C, increased *NFIA* expression, and improved Montreal Cognitive Assessment scores, especially in T2D-MCI patients. HDL-C rebounded at six months. In vitro, *NFIA* overexpression increased intracellular HDL-C and suppressed NF-κB signaling, while *NFIA* knockdown reduced APOA1 and APOE.

Conclusions: HDL-C has divergent genetic effects on T2D and MCI. *NFIA* modulates HDL-C and NF-κB activity, supporting metabolic and cognitive improvements. Targeting *NFIA* through MFT may represent a promising strategy for T2D-MCI prevention and treatment.

Keywords: Type 2 diabetes; Mild cognitive impairment; HDL-C; NHANES; Mendelian randomization

1. Introduction

Type 2 diabetes (T2D) is a chronic metabolic disorder characterized by persistent hyperglycemia, primarily driven by insulin resistance and β-cell dysfunction, with both genetic and environmental contributors[1]. Its growing prevalence—particularly among older adults—substantially increases the risk of cardiovascular disease, kidney dysfunction, dementia, and other complications, resulting in significant healthcare and economic burdens. For instance, in China, diabetes-related healthcare costs are projected to rise from 250.2 billion yuan in 2020 to 460.4 billion yuan by 2030, an average annual increase of 6.32%[2]. As disease management advances, attention is increasingly turning to previously overlooked comorbidities, including cognitive decline, cancer, and depression[3].

Mild cognitive impairment (MCI), a clinical state between normal aging and dementia, is closely linked to neurodegenerative diseases such as Alzheimer's and Parkinson's[4]. Metabolic abnormalities—such as T2D, prediabetes, and impaired glucose regulation—accelerate cognitive decline through mitochondrial dysfunction, chronic inflammation, vascular damage, and neuronal loss[5-7]. Greater amyloid burden was associated with increased functional impairment, but this relationship was observed only in Veterans with T2DM[8]. Emerging research indicates that fasting may enhance insulin sensitivity, promote β-cell regeneration, and improve glycemic control[9, 10]. Animal studies further suggest fasting supports memory, motor function, and hippocampal neurogenesis, highlighting its potential in treating both T2D and MCI[11].

T2D commonly coexists with dyslipidemia, typically characterized by elevated triglycerides (TG), reduced high-density lipoprotein cholesterol (HDL-C), and increased low-density lipoprotein cholesterol (LDL-C)[12]. HDL-C facilitates reverse cholesterol transport and provides vascular protection through anti-inflammatory, antioxidant, and antithrombotic effects[13]. In T2D, high TG levels enhance cholesteryl ester transfer protein activity, lowering HDL-C further and impairing insulin secretion and glucose uptake[14]. Notably, small HDL particles can cross the blood–brain barrier, suggesting peripheral HDL-C levels may influence brain function. Higher HDL-C concentrations have been linked to a lower risk of cognitive decline, likely by reducing cerebrovascular inflammation and preserving neuronal activity[15].

Therefore, this study aimed to identify a shared biomarker for assessing the risk of T2D-related cognitive

impairment and to evaluate a non-pharmacological intervention for its regulation. We investigated the causal role of HDL-C and its regulatory gene at the metabolic-cognitive interface. This integrated approach provides novel insights into potential strategies for the prevention and treatment of comorbid T2D and MCI.

2. Materials and methods

2.1. Study design

The study was structured in four stages. Initially, disease-associated indicators were identified by comparing individuals with T2D and MCI to healthy controls, using data from the National Health and Nutrition Examination Survey (NHANES). Genetic causality of key indicators was subsequently assessed through Mendelian randomization (MR), supported by transcriptomic analysis. The clinical efficacy of modified fasting therapy (MFT) was then evaluated in a prospective cohort. Finally, functional validation of candidate genes was carried out through cellular experiments.

2.2. NHANES data analysis

NHANES datasets from 1999 to 2018 were analyzed to evaluate health and nutritional status. Participants were excluded if aged under 18, missing essential clinical variables, or lacking survival information. For MCI-related analysis, only individuals with valid Digit Symbol Substitution Test (DSST) scores were included (***Supplementary Fig. 1***).

2.3. Definitions of T2D and prediabetes

T2D was defined by hemoglobin A1c (HbA1c) levels ≥6.5% or current use of glucose-lowering medication. Prediabetes was defined by HbA1c levels ranging from 5.7% to 6.5%. Participants not meeting either criterion were classified as normoglycemic[16, 17].

2.4. MCI diagnosis

MCI was defined in individuals aged ≥65 years with DSST scores within the lowest quartile during the 1999–2000, 2001–2002, 2011–2012, or 2013–2014 NHANES cycles[18].

2.5. Statistical analysis of NHANES

Statistical analyses were conducted using R software (version 4.2.3) with the application of appropriate survey weights. Continuous variables were reported as means ± standard deviations or medians with

interquartile ranges, while categorical variables were expressed as percentages. Group comparisons were performed using Chi-square tests for categorical variables and ANOVA or Kruskal–Wallis tests for continuous variables. Spearman correlation was employed to examine associations. Statistical significance was defined as $p < 0.05$.

2.6. Mendelian randomization

A Two-sample MR analysis was conducted using single nucleotide polymorphisms (SNPs) from the GWAS Catalog, filtered by genome-wide significance ($p < 5\times10^{-8}$), low linkage disequilibrium ($r^2 < 0.05$), and a 10,000 kb window. Alzheimer's GWAS summary statistics were used as a proxy for MCI. SNPs associated with confounders were excluded using LDlink. The inverse-variance weighted (IVW) method was used as the primary analytic approach, complemented by MR-Egger regression, weighted median, and mode-based estimators. Horizontal pleiotropy and heterogeneity were assessed using the MR-Egger intercept, Cochran's Q test, and MR-PRESSO. All analyses were performed using the "TwoSampleMR" and "MRPRESSO" R packages (***Supplementary Table 1***).

2.7. Transcriptomic analysis

The RNA-seq datasets from peripheral blood samples of patients with type 2 diabetes in the GEO database (GSE151683, GSE19790, GSE23561, GSE41767, and GSE69528; n = 151) were analyzed. Differentially expressed genes (DEGs) were identified using the "limma" and "sva" packages, applying thresholds of $|\log_2FC| > 0.3$ and $p < 0.05$. Heatmaps were generated using the "pheatmap" package. Functional enrichment analysis was performed with "clusterProfiler", "org.Hs.eg.db". HDL-C–related genes were retrieved from the GeneCards database.

2.8. Modified fasting therapy

MFT was implemented in three phases: (1) a 1–2 day pre-fasting period with a fruit-only diet; (2) a 5-day fasting phase with ≤550 kcal/day and 3 L/day of water or herbal tea; and (3) a structured refeeding phase. Intravenous L-carnitine (2 g, twice daily) was administered to reduce hunger and promote lipid metabolism[19-21].

2.9. Patient recruitment and data collection

A total of 27 patients diagnosed with type 2 diabetes were recruited from the Seventh Affiliated Hospital of Sun Yat-sen University (Ethics Approval No. KY-2021-108-01). Informed consent was obtained from all participants. Clinical parameters, laboratory results, and cognitive assessments were collected before and after the intervention. Diabetes diagnoses were established according to standardized clinical criteria[16].

2.10. Cognitive assessment

Cognitive function was assessed pre- and post-intervention using the Montreal Cognitive Assessment (MoCA) and the DSST. MoCA scores below 26 were interpreted as indicative of cognitive impairment. Higher DSST scores were considered reflective of better cognitive performance[22].

2.11. Transcriptome sequencing

Total RNA was extracted using Vazyme reagents, quantified with Nanodrop and Qubit instruments, and assessed for integrity. Sequencing libraries with approximately 300 bp inserts were prepared and sequenced on the Illumina NovaSeq 6000 platform. Sequence reads were aligned to the human reference genome, and differential expression analysis was conducted using the "DESeq2" package.

2.12. Cell culture

HepG2 and 293T cells were maintained in DMEM supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin at 37°C in a 5% CO_2 incubator. SH-SY5Y cells were maintained in DMEM/F12 with the same supplements and conditions. Cells were seeded at 60–80% confluency prior to experimental procedures.

2.13. Western blotting

Proteins were extracted, separated by SDS-PAGE, and transferred to PVDF membranes. Immunoblotting was performed using primary antibodies against NFIA, p65, phosphorylated p65 (p-p65), IκBα, phosphorylated IκBα (p-IκBα), and GAPDH (Cell Signaling Technology). Detection was carried out using HRP-conjugated secondary antibodies (ABclonal) and enhanced chemiluminescence reagents (Vazyme).

2.14. Quantitative RT-PCR

Complementary DNA was synthesized using the HiScript III RT Kit (Vazyme). Quantitative PCR was performed with SYBR Green Master Mix (Vazyme). Relative gene expression was normalized to GAPDH

and calculated using the $2^{-\Delta\Delta Ct}$ method. Primer sequences are provided in ***Supplementary Table 2.***

2.15. Detection of intracellular HDL-C

Cells were washed with PBS, lysed via sonication, and analyzed using a commercial HDL-C assay kit (Nanjing Jiancheng) following the manufacturer's protocol.

2.16. Nuclear Factor I A (*NFIA*) siRNA and overexpression plasmid transfection

HepG2 and SH-SY5Y cells were transfected with either *NFIA*-specific siRNA (si-*NFIA*) or negative control siRNA (si-NC) or a plasmid encoding *NFIA* for overexpression using Lipofectamine 3000 (Invitrogen), following the manufacturer's instructions. Plasmid DNA or siRNA and transfection reagent were diluted in Opti-MEM, incubated for complex formation, and applied to cells. After 6 h, the medium was replaced. Cells were harvested 48 h post-transfection for subsequent qPCR and Western blot analysis.

2.17. APOE and APOA1 quantification by enzyme-linked immunosorbent assay (ELISA)

Cellular APOE and APOA1 levels were measured using ELISA kits (FineTest). After lysis, samples were centrifuged at 1000 × g for 10 min at 4°C to remove debris. Supernatants (100 µL) and standards were added to antibody-coated 96-well plates and incubated at 37°C for 1.5 h. Following washing, 100 µL of detection antibody was added and incubated for another hour. After additional washes, 100 µL of HRP-conjugated secondary antibody was applied and incubated for 30 min. Then 90 µLSubstrate solution was added and incubated in the dark for 10–20 min. Reactions were stopped with 50 µL of stop solution. Absorbance was measured at 450 nm, and concentrations were calculated using standard curves.

2.18. Statistical analysis

Data were analyzed using *t*-tests or Mann-Whitney *U* tests for two-group comparisons, and one-way ANOVA or Kruskal-Wallis tests with post hoc analysis for multiple groups. Paired *t*-tests or Wilcoxon signed-rank tests were used for pre- vs post-treatment comparisons. Statistical significance was defined as $p < 0.05$.

3. Results

3.1. Baseline characteristics

This study included 49,078 participants (23,916 men and 25,169 women), categorized as normal, prediabetic, or T2D based on HbA1c levels and medication use. As summarized in ***Table 1***, 66.4% were

normal (n = 32,586), 20.7% prediabetic (n = 10,316), and 13.0% T2D (n = 6,356). Mean age increased significantly across groups (41.78, 55.67 and 58.86 years; $p < 0.001$). Most participants were non-Hispanic White with a high school education. The prevalence of hypertension, overweight/obesity, and central obesity, as well as mean values of blood pressure, BMI, waist circumference, triglycerides, and HbA1c all differed significantly among groups ($p < 0.001$).

Cognitive data were available for 5,011 individuals (2,539 women, 2,471 men), of whom 1,138 (22.7%) were classified with MCI and 3,873 (77.3%) as cognitively normal. As shown in ***Table 1***, the MCI group was older and had lower educational attainment, consistent with prior studies[23]. HbA1c levels and rates of hypertension and T2D were significantly higher in the MCI group, while BMI and overweight/obesity status showed no significant differences.

3.2. Observational analysis of T2D and MCI indicators in NHANES

NHANES examination and laboratory data were analyzed by quartiles (***Supplementary Table 3***). Q4 values were used for comparative analysis of T2D and MCI-related biomarkers (***Supplementary Table 4***) as well as for subgroup analysis (***Supplementary Tables 5-8***). Most biomarkers varied significantly across T2D groups ($p < 0.001$), while fewer differences were observed in MCI. Shared indicators are listed in ***Table 2***. This disparity likely reflects the systemic nature of T2D—characterized by metabolic dysfunction and multi-organ involvement—whereas MCI is primarily a neurocognitive condition with more localized physiological effects.

3.3. Correlation between key biomarkers and T2D or MCI

Indicators showing significant group differences were further analyzed for correlations with T2D and MCI outcomes. As anticipated, glycohemoglobin, fasting glucose, C-peptide, and two-hour plasma glucose were strongly correlated with T2D ($r > 0.55$, $p < 0.01$) (***Supplementary Table 9***). Blood urea nitrogen and red cell distribution width also showed positive correlations ($r > 0.4$) (***Fig. 1A***). In the MCI group, globulin levels were positively associated ($r > 0.4$), whereas vitamin D and creatinine were negatively correlated ($r < -0.3$). These moderate correlations ($r = 0.3 - 0.5$) indicate potential biochemical differences in cognitive impairment, though their clinical significance is limited.

3.4. Causal effects of HDL-C on T2D and MCI: mendelian randomization analysis

Given the established causal role of blood glucose and insulin in T2D, we investigated additional factors potentially influencing both T2D and MCI. Biomarkers significantly correlated with either condition ($|r| > 0.3$, $p < 0.05$), such as direct HDL-C and uric acid, were selected for MR to assess potential causality.

As presented in ***Table 3***, IVW MR identified a significant causal link between HDL-C and both outcomes. Genetically higher HDL-C levels were associated with a lower risk of T2D (odds ratio [OR] = 0.9059, 95% CI: 0.8666–0.9470) but a higher risk of MCI (OR = 1.0482, 95% CI: 1.0216–1.0755). These results were consistent across four additional MR methods, reinforcing their reliability ***(Fig. 1B-C)***.

MR-Egger analysis revealed significant heterogeneity in HDL-C's effects on T2D ($p = 1.10 \times 10^{-8}$) and MCI ($p = 0.0367$), prompting the use of a multiplicative random-effects IVW model to account for this variability. Tests for horizontal pleiotropy using MR-Egger ($p > 0.05$) and MR-PRESSO indicated potential pleiotropy but detected no outlier SNPs. Leave-one-out analysis confirmed that the associations were not driven by any single SNP but rather reflected contributions from multiple variants. ***Supplementary Fig. 2*** and ***Supplementary Table 10*** provide detailed SNP information and MR results for other biomarkers.

3.5. Transcriptomic profiling and identification of HDL-C-related targets in T2D

To identify molecular targets linking HDL-C and T2D, transcriptomic analysis was performed using 151 samples from five GEO datasets. Batch effects were corrected before downstream analysis (***Supplementary Fig. 3A-B***). In total, 552 DEGs were identified in the T2D group compared to non-diabetic (ND) controls, with 232 genes upregulated and 320 downregulated (***Fig. 1D***). KEGG analysis of the DEGs revealed significant enrichment in pathways such as mitophagy, PI3K-Akt signaling, autophagy, cholinergic synapse, and apoptosis **(*Supplementary Fig. 3C*)**. In parallel, GSEA demonstrated that these DEGs were closely associated with Alzheimer's disease (AD) **(*Fig. 1E*)**, suggesting a potential link between T2D and increased risk of AD.

To further explore HDL-C-related genes implicated in T2D, genes associated with HDL-C (GeneCards relevance score $\geqslant 1$, ***Supplementary Table 11***) were cross-referenced with T2D DEGs and SNP-annotated loci. This integrative approach identified one candidate gene, *NFIA* (***Fig. 1F***), potentially bridging HDL-C

regulation with T2D pathogenesis.

3.6. Therapeutic effects of MFT on T2D and MCI

Forty participants (17 with T2D and 23 controls) completed the MFT intervention. Baseline characteristics are provided in ***Supplementary Table 12***. Post-MFT, significant reductions were observed in BMI ($p < 0.0001$), fasting blood glucose (FBG; $p < 0.0006$), and HDL-C ($p < 0.0001$), while β-hydroxybutyrate (β-HB) levels rose markedly ($p < 0.0001$)***(Fig.2A-D)***. FBG decreased more substantially in the T2D group compared to controls ($p = 0.0199$) (***Supplementary Fig. 4A***). At three and six months, HDL-C levels rebounded above both baseline and immediate post-fasting levels (***Fig. 2E-F***). Cognitive function was assessed using the MoCA ($n = 31$) and the DSST ($n = 27$). Baseline MoCA scores were lower in the T2D group than in controls ($p = 0.0248$) (***Fig. 2G***). Following MFT, MoCA scores improved significantly overall, with the most pronounced gains observed in T2D patients with MCI ($p = 0.0109$) (***Fig. 2J***). DSST scores also improved in this subgroup ($p = 0.0237$) (***Fig. 2I***), although group-level changes were not statistically significant (***Supplementary Fig. 4B, C***). These results indicate that T2D is associated with elevated MCI risk, and that MFT can enhance both metabolic and cognitive outcomes, especially in patients with comorbid T2D and MCI.

Expression of *NFIA*, a key gene identified through prior analyses, was significantly upregulated after MFT ($p = 0.0002$), particularly in participants with T2D ($p = 0.0004$) and MCI ($p = 0.001$), whereas changes in controls did not reach statistical significance ($p = 0.098$) (***Fig. 2K***, ***Supplementary Fig. 4D-F***).

3.7. Transcriptomic analysis of MFT response

Peripheral blood RNA-seq was performed on samples from eleven randomly selected participants (5 T2D and 6 control) before and after MFT. Using thresholds of $|\log_2 FC| > 0.3$ and $p < 0.05$, we identified 447 upregulated and 246 downregulated DEGs post-MFT (***Fig. 3A, Supplementary Table 13***), with *NFIA* among the upregulated genes. KEGG enrichment analysis revealed that upregulated DEGs were involved in pathways related to unsaturated fatty acid biosynthesis, fatty acid metabolism, and PI3K-Akt signaling, suggesting that MFT may improve metabolic function and insulin sensitivity through these molecular pathways (***Fig. 3B, Supplementary Fig. 5***).

3.8. Functional role of *NFIA* in HepG2 and SH-SY5Y cells

The *NFIA* gene plays a key role in the regulation of HDL-C, which is primarily synthesized in the liver[24]. To investigate its function, we overexpressed *NFIA* in HepG2 cells. Overexpression was confirmed via qPCR and Western blotting (***Supplementary Fig. 6A-B***). Intracellular HDL-C levels were significantly higher in *NFIA*-overexpressing cells compared to controls ($p = 0.0002$; ***Fig. 3C***). Additionally, *NFIA* overexpression reduced phosphorylation of NF-κB p65 and IκBα, indicating inhibition of the NF-κB signaling pathway (***Fig. 3D-F)***. These findings suggest a potential anti-inflammatory mechanism. At the same time, following *NFIA* knockdown in HepG2 and SH-SY5Y cells (***Supplementary Fig. 6C-D***), ELISA results showed decreased levels of APOA1 (HepG2: $p = 0.0228$; SH-SY5Y: $p = 0.0014$) and APOE (HepG2: $p = 0.0097$; SH-SY5Y: $p = 0.0023$) **(*Fig. 3G-J, Supplementary Fig. 6E-F*)**. These findings suggest that *NFIA* may play a regulatory role in HDL-C biosynthesis.

4. Discussion

Mounting evidence indicates a shared pathogenic pathway between T2D and MCI, driven largely by hyperglycemia, chronic inflammation, and neuronal dysfunction[25-27]. Hyperglycemia promotes systemic inflammation, contributing to widespread tissue damage, including the brain.

NHANES data revealed significant differences in serum vitamin D, globulin, and HDL-C levels among individuals with T2D, MCI, and healthy controls. MR analysis showed that genetically elevated HDL-C is linked to a lower risk of T2D but a higher risk of MCI. Vitamin D levels were inversely associated with both conditions. Supplementation may reduce the incidence of T2D and MCI, even in patients with existing diabetes. This protective effect is likely mediated by the regulatory role of vitamin D in insulin signaling, particularly through inhibition of pathways such as NF-κB and TLR4[28]. Vitamin D receptors in pancreatic β-cells, skeletal muscle, and adipose tissue enhance insulin sensitivity and preserve β-cell function, slowing T2D progression[29]. Additionally, vitamin D supports neuroprotection, calcium balance, antioxidant activity, and anti-inflammatory processes[30]. Clinical studies associate higher serum vitamin D levels in older adults with better cognitive function[31].

An apparent contradiction exists regarding HDL-C. NHANES data suggest higher HDL-C is protective against MCI, while MR analyses indicate genetically elevated HDL-C increases MCI risk. This discrepancy stems from methodological differences: MR reflects lifelong genetic exposure and minimizes confounding and reverse causality[32, 33], whereas NHANES offers cross-sectional snapshots influenced by age, lifestyle, and comorbidities[34]. Moreover, HDL composition differs between the central nervous system (CNS) and periphery. CNS HDL includes peripheral APOA1 and glial-derived APOE. The APOE4 isoform, a major genetic risk factor for neurodegeneration, promotes amyloid-β accumulation, tau pathology, and blood–brain barrier disruption[35, 36]. Therefore, if peripheral HDL-C primarily reflects APOA1 rather than APOE, the protective association observed in NHANES remains biologically plausible.

To account for genetic effects driven by *APOE*, *APOEε4*-related SNPs were excluded in the two-sample MR analysis. Nonetheless, a direct positive causal relationship between HDL-C and MCI was still observed. This may be attributed to the fact that APOE4 protein levels are regulated not only at the transcriptional level by *APOEε4* but also through post-transcriptional mechanisms. While genes involved in these regulatory processes may not directly cause MCI, they could influence disease progression by modulating APOE4 expression. In addition, HDL undergoes post-translational modifications that can generate functionally abnormal forms such as oxidized HDL and acetylated HDL[37, 38]. These altered HDL particles may induce endothelial dysfunction and elevate inflammation through multiple pathways, thereby contributing to neuronal injury and cognitive decline.

Conventional lipid-lowering therapies have limited efficacy in elevating HDL-C. Although niacin can increase HDL-C levels, its use is restricted by adverse side effects. As an alternative, we implemented MFT, a non-pharmacological intervention widely used in the management of obesity and diabetes. MFT enhances fatty acid mobilization and ketone body production, providing an alternative energy source—particularly for the brain—during fasting states[39]. Mild hyperketonemia, induced by fasting or ketogenic diets, has been shown to regulate inflammation, oxidative stress[40], glucose metabolism, insulin sensitivity, and synaptic plasticity[41, 42], thereby improving cognitive and motor function[43, 44]. In our MFT cohort, short-term improvements were observed in FBG, β-HB, and cognitive performance. Although HDL-C levels initially

declined post-intervention, they increased significantly at six months, consistent with findings by Longo and Frigeri[45, 46].

Genome-wide association and transcriptomic analyses identified *NFIA* as a key regulator of HDL-C metabolism. Following MFT, *NFIA* expression was markedly upregulated in peripheral blood. *NFIA* has been shown to enhance circulating HDL-C[47, 48], suppress pro-inflammatory cytokines[49], and protect against hyperglycemia and weight gain in high-fat diet models[50]. It also plays a role in mitigating T2D and obesity-related metabolic dysfunction[47]. In vitro, *NFIA* overexpression elevated HDL-C levels and inhibited classical NF-κB signaling, suggesting dual roles in lipid regulation and inflammation. These results indicate that MFT may exert its beneficial effects, in part, through *NFIA*-mediated pathways. Given the lack of effective treatments for MCI, MFT offers a safe and promising strategy with therapeutic potential for both metabolic and cognitive disorders.

Despite the novel association we report between NFIA expression and MCI in T2D, its immediate clinical translatability is limited. NFIA remains a tissue-level transcription factor without validated circulating assays or prospective cohort data supporting its biomarker role. Moreover, the observed relationship between higher HDL-C and increased MCI risk in our cohort likely reflects qualitative HDL dysfunction rather than a true deleterious effect of cholesterol-rich lipoproteins. In T2D, HDL undergoes glycation and oxidative modifications—mediated in part by myeloperoxidase—that impair cholesterol efflux capacity and confer pro-inflammatory properties, potentially exacerbating neuroinflammation and cognitive decline[51, 52]. Thus, future studies should focus on assays of HDL functionality rather than HDL-C levels alone. Finally, although intermittent fasting has garnered considerable interest, large randomized trials demonstrate that its benefits for weight loss and metabolic health are not superior to those achieved by equivalent caloric restriction[53]. However, intermittent fasting may be more feasible over the long term than continuous caloric restriction[54], and Paul J Arciero *et al*. have shown that it is more effective at reducing visceral fat[55]. As such， the mechanistic impact of fasting regimens on HDL quality and neuroprotection in diabetic patients warrants rigorous, targeted investigation.

This study has several limitations. First, in the NHANES analysis, the number of participants who completed the DSST cognitive test was limited, resulting in a smaller MCI group compared to the T2D group. Second, the clinical study of MFT lacked longitudinal cognitive follow-up, which precluded the evaluation of its long-term effects on memory.

5. Conclusion

We identified HDL-C as an independent factor linked to both T2D and MCI, and observed significant alterations in *NFIA* expression among individuals with T2D. MFT, a non-pharmacological dietary intervention, was found to upregulate *NFIA*, leading to sustained increases in HDL-C, suppression of NF-κB signaling, and concurrent improvements in glycemic control and cognitive performance—particularly in T2D patients with MCI. These results suggest that *NFIA* and HDL-C may serve as dual biomarkers for early detection of metabolic-cognitive comorbidity. MFT offers a safe, practical approach to modulate this pathway. Further longitudinal studies in diverse populations are warranted to validate these findings and assess the potential of *NFIA*-targeted strategies in personalized prevention and treatment of T2D and MCI.

Ethics Statement: Ethics approval was granted by the Ethics Committee of the Seventh Affiliated Hospital, Sun Yat-sen University (KY-2021-108-01).

Conflicts of Interest: The authors declare no competing interests.

Funding: This work was supported by the Traditional Chinese Medicine Bureau of Guangdong Province (no. 20231077); Basic and Applied Basic Research Foundation of Guangdong Province (no.2022A1515220096); Shenzhen Fundamental Research Program (no. JCYJ20230807110417036); Shenzhen Key Laboratory of Chinese Medicine Active substance screening and Translational Research (ZDSYS20220606100801003, NO. SKLCMASSTR202404M).

Abbreviation

AD: *Alzheimer's disease*

BP: *Biological process*

BMI: *Body mass index*

CC: *Cellular component*

DBP: *Diastolic blood pressure*

DEGs: *Differentially expressed genes*

DSST: *Digit symbol substitution test*

FBG: *Fasting blood glucose*

GWAS: *Genome-wide association study*

HbA1c: *Glycated hemoglobin*

HDL: *High-density lipoprotein*

HDL-C: *High-density lipoprotein cholesterol*

IVW: *Inverse-variance weighted*

LDL-C: *Low-density lipoprotein cholesterol*

MR: *Mendelian randomization*

MCI: *Mild cognitive impairment*

MEC: *Mobile examination center*

MFT: *Modified fasting therapy*

MF: *Molecular function*

MOCA: *Montreal Cognitive Assessment*

NHANES: *National Health and Nutrition Examination Survey*

NDD: *Neurodegenerative disorders*

ND: *Non-diseased*

OGTT: *Oral glucose tolerance test*

SBP: *Systolic blood pressure*

TG: *Triglyceride*

T2D: *Type 2 diabetes*

β-HB: *β-hydroxybutyrate*

Reference

[1]. Eizirik, D.L., L. Pasquali, and M. Cnop, *Pancreatic beta-cells in type 1 and type 2 diabetes mellitus: different pathways to failure.* Nat Rev Endocrinol, 2020. **16**(7): p. 349-362.

[2]. Liu, J., et al., *Projected rapid growth in diabetes disease burden and economic burden in China: a spatio-temporal study from 2020 to 2030.* Lancet Reg Health West Pac, 2023. **33**: p. 100700.
[3]. Tomic, D., J.E. Shaw, and D.J. Magliano, *The burden and risks of emerging complications of diabetes mellitus.* Nat Rev Endocrinol, 2022. **18**(9): p. 525-539.
[4]. Baiano, C., et al., *Prevalence and clinical aspects of mild cognitive impairment in Parkinson's disease: A meta-analysis.* Mov Disord, 2020. **35**(1): p. 45-54.
[5]. Xue, M., et al., *Diabetes mellitus and risks of cognitive impairment and dementia: A systematic review and meta-analysis of 144 prospective studies.* Ageing Res Rev, 2019. **55**: p. 100944.
[6]. Biessels, G.J. and F. Despa, *Cognitive decline and dementia in diabetes mellitus: mechanisms and clinical implications.* Nat Rev Endocrinol, 2018. **14**(10): p. 591-604.
[7]. Shen, Z., et al., *Metabolic perspective of astrocyte dysfunction in Alzheimer's disease and type 2 diabetes brains.* Biomed Pharmacother, 2023. **158**: p. 114206.
[8]. Alshaheri Durazo, A., et al., *Type 2 Diabetes Moderates the Association Between Amyloid and 1-Year Change in Everyday Functioning in Older Veterans.* J Alzheimers Dis, 2024. **97**(1): p. 219-228.
[9]. Brandhorst, S., et al., *Fasting-mimicking diet causes hepatic and blood markers changes indicating reduced biological age and disease risk.* Nat Commun, 2024. **15**(1): p. 1309.
[10]. Cheng, C.W., et al., *Fasting-Mimicking Diet Promotes Ngn3-Driven beta-Cell Regeneration to Reverse Diabetes.* Cell, 2017. **168**(5): p. 775-788 e12.
[11]. Brandhorst, S., et al., *A Periodic Diet that Mimics Fasting Promotes Multi-System Regeneration, Enhanced Cognitive Performance, and Healthspan.* Cell Metab, 2015. **22**(1): p. 86-99.
[12]. Kane, J.P., et al., *Dyslipidemia and diabetes mellitus: Role of lipoprotein species and interrelated pathways of lipid metabolism in diabetes mellitus.* Curr Opin Pharmacol, 2021. **61**: p. 21-27.
[13]. Poliakova, T. and C.L. Wellington, *Roles of peripheral lipoproteins and cholesteryl ester transfer protein in the vascular contributions to cognitive impairment and dementia.* Mol Neurodegener, 2023. **18**(1): p. 86.
[14]. von Eckardstein, A., et al., *High-density lipoprotein revisited: biological functions and clinical relevance.* Eur Heart J, 2023. **44**(16): p. 1394-1407.
[15]. Vitali, C., C.L. Wellington, and L. Calabresi, *HDL and cholesterol handling in the brain.* Cardiovasc Res, 2014. **103**(3): p. 405-13.
[16]. American Diabetes, A., *2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020.* Diabetes Care, 2020. **43**(Suppl 1): p. S14-S31.
[17]. Ciardullo, S. and G. Perseghin, *Statin use is associated with lower prevalence of advanced liver fibrosis in patients with type 2 diabetes.* Metabolism, 2021. **121**: p. 154752.
[18]. Chen, S.P., J. Bhattacharya, and S. Pershing, *Association of Vision Loss With Cognition in Older Adults.* JAMA Ophthalmol, 2017. **135**(9): p. 963-970.
[19]. Virmani, M.A. and M. Cirulli, *The Role of l-Carnitine in Mitochondria, Prevention of Metabolic Inflexibility and Disease Initiation.* Int J Mol Sci, 2022. **23**(5).
[20]. Zhang, T., et al., *L-carnitine ameliorated weight loss in fasting therapy: A propensity score-matched study.* Complement Ther Med, 2019. **44**: p. 162-165.

[21]. Liu, T., et al., *Efficacy and safety of modified fasting therapy for weight loss in 2054 hospitalized patients.* Obesity (Silver Spring), 2023. **31**(6): p. 1514-1529.
[22]. Cukierman-Yaffe, T., et al., *Effect of dulaglutide on cognitive impairment in type 2 diabetes: an exploratory analysis of the REWIND trial.* Lancet Neurol, 2020. **19**(7): p. 582-590.
[23]. Lovden, M., et al., *Education and Cognitive Functioning Across the Life Span.* Psychol Sci Public Interest, 2020. **21**(1): p. 6-41.
[24]. Han, Y.H., et al., *Enterically derived high-density lipoprotein restrains liver injury through the portal vein.* Science, 2021. **373**(6553).
[25]. Little, K., et al., *Common pathways in dementia and diabetic retinopathy: understanding the mechanisms of diabetes-related cognitive decline.* Trends Endocrinol Metab, 2022. **33**(1): p. 50-71.
[26]. Dewanjee, S., et al., *Altered glucose metabolism in Alzheimer's disease: Role of mitochondrial dysfunction and oxidative stress.* Free Radic Biol Med, 2022. **193**(Pt 1): p. 134-157.
[27]. Zhang, S., et al., *Glucose metabolic crosstalk and regulation in brain function and diseases.* Prog Neurobiol, 2021. **204**: p. 102089.
[28]. Dong, B., et al., *Vitamin D Receptor Activation in Liver Macrophages Ameliorates Hepatic Inflammation, Steatosis, and Insulin Resistance in Mice.* Hepatology, 2020. **71**(5): p. 1559-1574.
[29]. Pittas, A.G., et al., *Vitamin D and Risk for Type 2 Diabetes in People With Prediabetes : A Systematic Review and Meta-analysis of Individual Participant Data From 3 Randomized Clinical Trials.* Ann Intern Med, 2023. **176**(3): p. 355-363.
[30]. Gall, Z. and O. Szekely, *Role of Vitamin D in Cognitive Dysfunction: New Molecular Concepts and Discrepancies between Animal and Human Findings.* Nutrients, 2021. **13**(11).
[31]. Scarmeas, N., C.A. Anastasiou, and M. Yannakoulia, *Nutrition and prevention of cognitive impairment.* Lancet Neurol, 2018. **17**(11): p. 1006-1015.
[32]. Holmes, M.V., M. Ala-Korpela, and G.D. Smith, *Mendelian randomization in cardiometabolic disease: challenges in evaluating causality.* Nat Rev Cardiol, 2017. **14**(10): p. 577-590.
[33]. Davies, N.M., M.V. Holmes, and G. Davey Smith, *Reading Mendelian randomisation studies: a guide, glossary, and checklist for clinicians.* BMJ, 2018. **362**: p. k601.
[34]. Li, Z., et al., *Higher Levels of Blood Selenium are Associated with Higher Levels of Serum Lipid Profile in US Adults with CKD: Results from NHANES 2013-2018.* Biol Trace Elem Res, 2023. **201**(12): p. 5501-5511.
[35]. Corder, E.H., et al., *Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's disease in late onset families.* Science, 1993. **261**(5123): p. 921-3.
[36]. Serrano-Pozo, A., S. Das, and B.T. Hyman, *APOE and Alzheimer's disease: advances in genetics, pathophysiology, and therapeutic approaches.* Lancet Neurol, 2021. **20**(1): p. 68-80.
[37]. Zhao, Y., et al., *Hydrogen sulfide upregulates SIRT1 to inhibit ox-HDL-induced endothelial cell damage and mitochondrial dysfunction.* Nitric Oxide, 2024. **152**: p. 78-89.
[38]. Speer, T., et al., *Abnormal high-density lipoprotein induces endothelial dysfunction via activation of Toll-like receptor-2.* Immunity, 2013. **38**(4): p. 754-68.
[39]. Jensen, N.J., et al., *Effects of Ketone Bodies on Brain Metabolism and Function in Neurodegenerative Diseases.* Int J Mol Sci, 2020. **21**(22).

[40]. Veneti, S., et al., *Ketone Bodies in Diabetes Mellitus: Friend or Foe?* Nutrients, 2023. **15**(20).
[41]. Gershuni, V.M., S.L. Yan, and V. Medici, *Nutritional Ketosis for Weight Management and Reversal of Metabolic Syndrome.* Curr Nutr Rep, 2018. **7**(3): p. 97-106.
[42]. Chung, J.Y., O.Y. Kim, and J. Song, *Role of ketone bodies in diabetes-induced dementia: sirtuins, insulin resistance, synaptic plasticity, mitochondrial dysfunction, and neurotransmitter.* Nutr Rev, 2022. **80**(4): p. 774-785.
[43]. Fortier, M., et al., *A ketogenic drink improves cognition in mild cognitive impairment: Results of a 6-month RCT.* Alzheimers Dement, 2021. **17**(3): p. 543-552.
[44]. Taylor, M.K., et al., *Feasibility and efficacy data from a ketogenic diet intervention in Alzheimer's disease.* Alzheimers Dement (N Y), 2018. **4**: p. 28-36.
[45]. Galetti, V., et al., *Observational Study of Lipid Profile and C-Reactive Protein after a Seven-Day Fast.* Nutrients, 2021. **13**(1).
[46]. Wei, M., et al., *Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease.* Sci Transl Med, 2017. **9**(377).
[47]. Hiraike, Y., et al., *NFIA co-localizes with PPARgamma and transcriptionally controls the brown fat gene program.* Nat Cell Biol, 2017. **19**(9): p. 1081-1092.
[48]. Zhao, J.J., et al., *Dihydrocapsaicin suppresses proinflammatory cytokines expression by enhancing nuclear factor IA in a NF-kappaB-dependent manner.* Arch Biochem Biophys, 2016. **604**: p. 27-35.
[49]. Hu, Y.W., et al., *RP5-833A20.1/miR-382-5p/NFIA-dependent signal transduction pathway contributes to the regulation of cholesterol homeostasis and inflammatory reaction.* Arterioscler Thromb Vasc Biol, 2015. **35**(1): p. 87-101.
[50]. Hiraike, Y., et al., *NFIA in adipocytes reciprocally regulates mitochondrial and inflammatory gene program to improve glucose homeostasis.* Proc Natl Acad Sci U S A, 2023. **120**(31): p. e2308750120.
[51]. Otocka-Kmiecik, A., et al., *Dysfunctional HDL: a novel important diagnostic and therapeutic target in cardiovascular disease?* Prog Lipid Res, 2012. **51**(4): p. 314-24.
[52]. Ganjali, S., et al., *HDL functionality in type 1 diabetes.* Atherosclerosis, 2017. **267**: p. 99-109.
[53]. Liu, D., et al., *Calorie Restriction with or without Time-Restricted Eating in Weight Loss.* N Engl J Med, 2022. **386**(16): p. 1495-1504.
[54]. James, D.L., et al., *Impact of Intermittent Fasting and/or Caloric Restriction on Aging-Related Outcomes in Adults: A Scoping Review of Randomized Controlled Trials.* Nutrients, 2024. **16**(2).
[55]. Arciero, P.J., et al., *Intermittent fasting and protein pacing are superior to caloric restriction for weight and visceral fat loss.* Obesity (Silver Spring), 2023. **31 Suppl 1**(Suppl 1): p. 139-149.

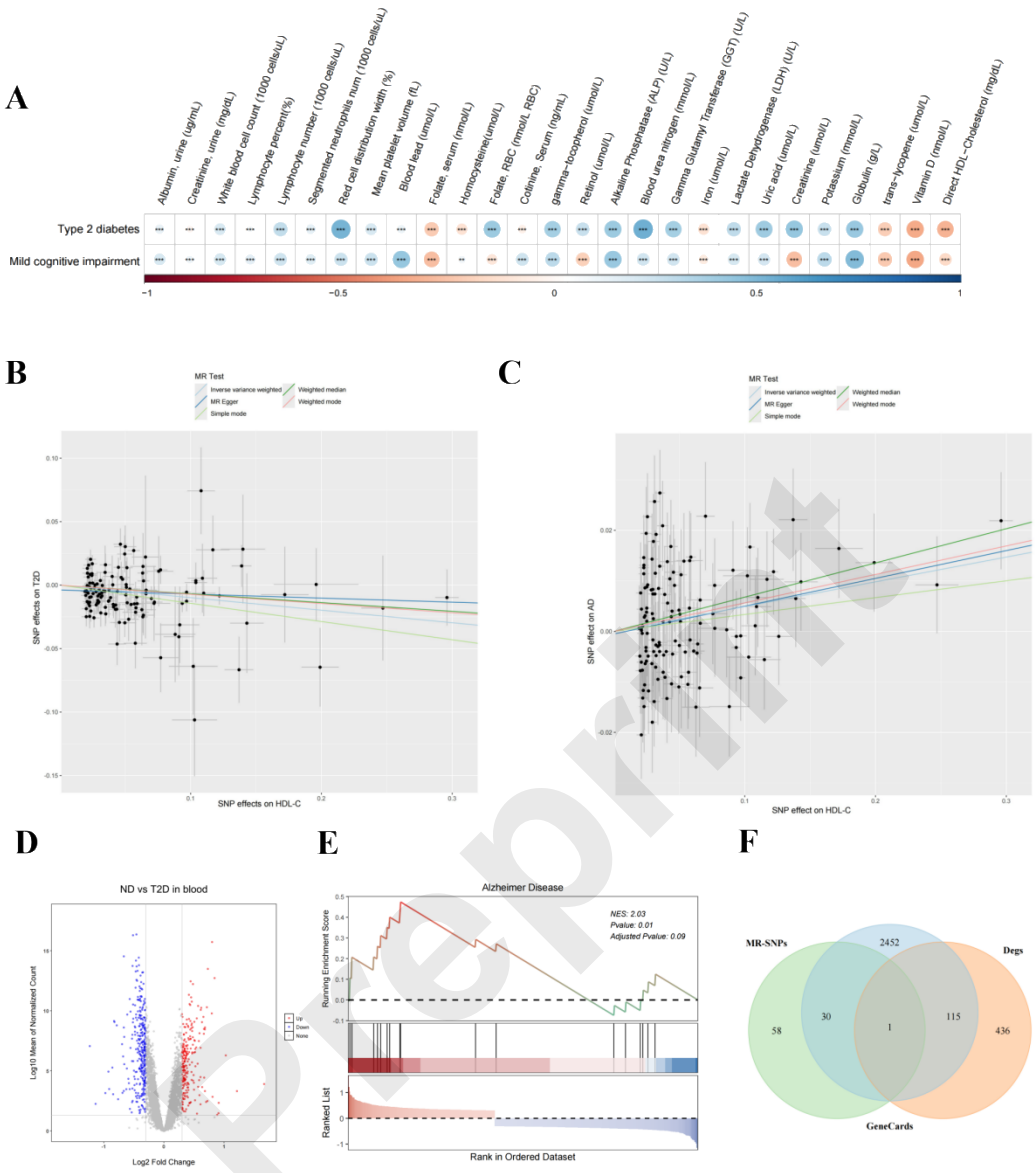


Figure 1. Integrated Analysis of Molecular Correlates and Gene Signatures in T2D, MCI, and AD; A. Correlation heatmap of differential indicators with T2D and MCI; B-C. Scatter plots showing the association between HDL-C and the risk of T2D and MCI; D. Distribution of upregulated and downregulated genes; E. GSEA enrichment plot for the Alzheimer disease-related gene set; F. Venn diagram showing the overlapping genes among ND-T2D DEGs (Orange), GeneCards (Blue), and MR-SNPs (Green). *p < 0.05, **p < 0.01, ***p < 0.001.

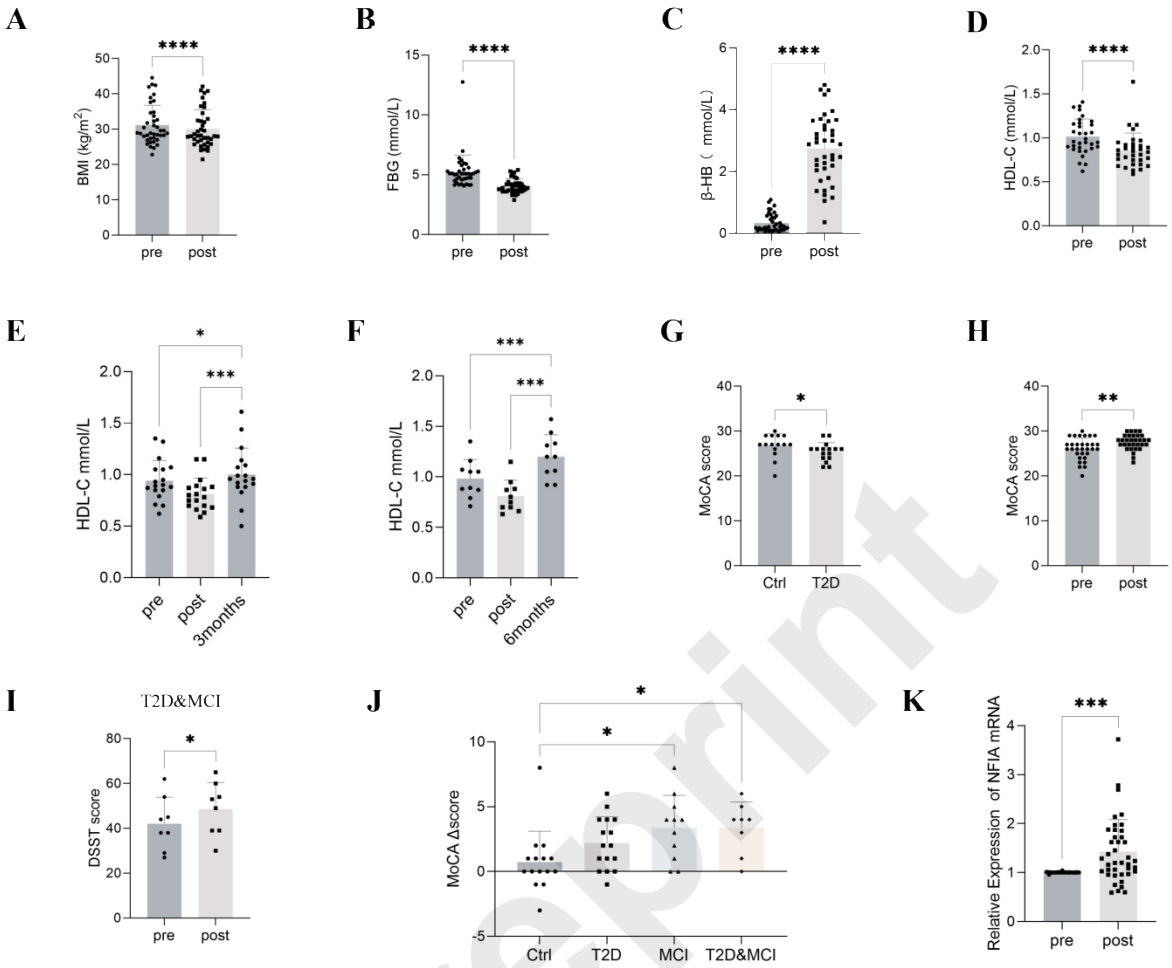


Figure 2. Analysis of key indicators pre- and post-MFT. A. BMI (n = 40); B. FBG (n = 40); C. β-HB (n = 40); D. HDL-C (n = 34); E. HDL-C levels were followed up for 3 months (n = 18); F. HDL-C levels were followed up for 3 months (n=10); G. Baseline MoCA scores (Ctrl: n = 15 , T2D: n = 16); H. MoCA score (n = 31); I. DSST scores in T2D&MCI group (n=8); J. MoCA score changes by group (Ctrl: n = 15, T2D: n = 16, MCI: n = 11, T2D&MCI: n = 8); K. NFIA expression in peripheral blood (n=40). Data presented as Mean ± SD. *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001.

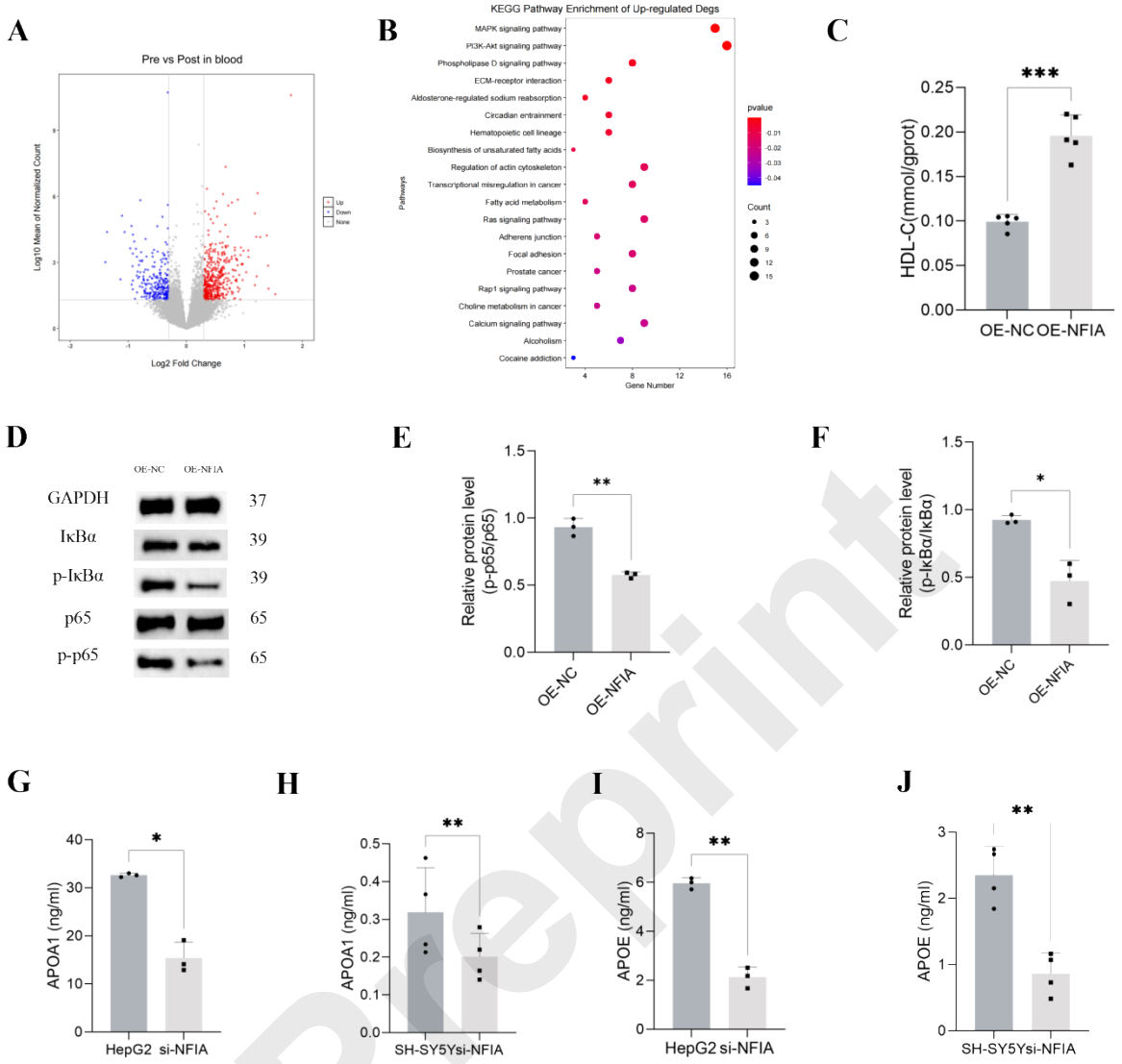


Figure 3. Transcriptomic and functional validation analyses related to NFIA. A.Volcano plot of DEGs in Peripheral Blood Before and After MFT; B. KEGG enrichment of Up-regulated DEGs; C. HDL-C levels in *NFIA*-overexpressing (OE-NFIA) HepG2 cells; D-F. Western Blotting analysis of NF-κB signaling pathway in OE-NFIA HepG2 cells; G. APOA1 levels in si-NFIA HepG2 cells; H. APOA1 levels in si-NFIA SH-SY5Y cells; I. APOE levels in si-NFIA HepG2 cells; J. APOE levels in si-NFIA SH-SY5Y cells. Data presented as Mean ± SD. *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001.

Table 1. Demographic and individual characteristics

		Normal	Prediabetes	T2D	p	Normal	MCI	p
		n=32586,66.40%	n=10136,20.65%	n=6356,12.95%		n=3873,77.30%	n=1138,22.70%	
GENDER, n(%)	Female	17042(51.5)	5049(52.2)	3076(48.2)	<0.001	2027(55.1)	512(54.1)	0.67
	Male	15544(48.5)	5087(47.8)	3280(51.8)		1846(44.9)	626(45.9)	
T2D (%)	normal	—	—	—	—	1859(51.9)	428(41.3)	<0.001
	prediabetes	—	—	—		1218(30.7)	364(29.2)	
	type 2 diabetes	—	—	—		796(17.5)	346(29.5)	
AGE, mean(SD)		41.78(16.17)	55.67(15.38)	58.86(13.83)	<0.001	69.01(6.69)	73.19(7.38)	<0.001
Race/Ethnicity, n(%)	Mexican American	6165(8.2)	1702(8.5)	1333(9.5)	<0.001	414(2.3)	299(9.0)	<0.001
	Other Hispanic	2522(5.5)	905(5.7)	598(6.1)		215(2.7)	157(13.2)	
	Non-Hispanic White	15318(71.2)	3849(62.4)	2166(60.5)		2341(85.3)	333(55.6)	
	Non-Hispanic Black	5769(8.8)	2706(15.6)	1635(15.0)		634(5.6)	306(18.4)	
	Other	2812(6.3)	974(7.7)	624(8.9)		269(4.1)	43(3.9)	
Education level, n(%)	<high school	8085(15.5)	3075(21.1)	2358(25.5)	<0.001	802(15.3)	787(59.1)	<0.001
	>high school	16655(60.7)	4554(51.9)	2571(49.5)		2072(59.0)	152(18.2)	
	high school	7819(23.7)	2496(26.9)	1418(25.0)		997(25.7)	194(22.3)	
	others	27(0.1)	10(0.1)	9(0.1)		2(0.0)	4(0.4)	
	NA	0(0.0)	1(0.0)	0.0(0.0)		0(0.0)	1(0.0)	
Hypertention, n(%)	normal	20645(63.1)	3419(35.9)	1080(17.9)	<0.001	773(21.4)	155(13.4)	<0.001
	hypertention	11941(36.9)	6717(64.1)	5276(82.1)		3100(78.6)	983(86.6)	
Obesity/Overweight, n(%)	normal	10121(30.3)	1534(14.9)	580(8.0)	<0.001	774(20.3)	228(22.2)	0.472
	overweight	13400(41.6)	4079(39.1)	2124(29.2)		45.5(44.4)	521(45.3)	
	obesity	9065(28.1)	4523(46.0)	3652(62.8)		34.5(35.2)	389(32.5)	
Central obesity, n(%)	normal	17812(54.0)	3321(30.1)	1343(17.6)		1377(32.6)	417(33.6)	0.628

	central obesity	14774(46.0)	6815(69.9)	5013(82.4)	<0.001	2496(67.4)	721(66.4)	
SBP(mmHg)		116.70[108.70,127.30]	125.30[115.30,137.30]	128.00[117.30,141.00]	<0.001	131.30[120.00,145.30]	139.30[126.00,155.86]	<0.001
DBP(mmHg)		70.70[64.00,78.00]	72.70[64.70,79.30]	70.70[62.00,78.00]	<0.001	70.70[62.70,77.30]	67.30[59.30,76.00]	<0.001
BMI(kg/m^2)		26.59[23.30,30.65]	29.30[25.76,34.00]	31.80[27.90,37.14]	<0.001	27.81[24.63,31.60]	27.60[24.20,31.53]	0.237
Waist Circumference (cm)		93.50[83.60,104.20]	102.40[93.20,112.30]	110.30[100.00,121.50]	<0.001	100.60[91.50,109.77]	100.10[91.50,109.50]	0.646
HbA1c (%)		5.20[5.00,5.40]	5.80[5.70,6.00]	7.00[6.40,8.10]	<0.001	5.60[5.40,6.00]	5.80[5.40,6.40]	<0.001

Table 2. Importent common differential laboratory characteristics

Terms	Normal	Prediabetes	T2D	p	Normal	MCI	p
Albumin,urine(ug/mL)	6.70[4.20,15.20]	6.90[4.40,19.90]	8.30[6.40,57.67]	<0.001	6.50[4.10,21.80]	8.90[6.00,53.81]	<0.001
Creatinine,urine(mg/dL)	80.00[49.00,207.00]	80.00[49.00,192.00]	83.00[52.00,172.00]	0.009	74.00[43.00,156.00]	80.00[50.00,175.00]	0.006
White blood cell count(1000cells/uL)	9.50[8.90,10.60]	9.80[9.10,11.00]	10.20[9.40,11.40]	<0.001	8.75[8.40,9.20]	9.10[8.60,9.44]	<0.001
Lymphocyte percent(%)	39.60[37.40,43.10]	40.80[38.20,44.90]	39.30[36.80,43.30]	<0.001	38.10[35.70,41.70]	39.20[36.58,43.53]	0.008
Lymphocyte number(1000cells/uL)	2.90[2.70,3.30]	3.10[2.80,3.50]	3.20[2.90,3.60]	<0.001	2.70[2.50,3.10]	2.90[2.60,3.30]	<0.001
Segmented neutrophils number(1000cells/uL)	6.10[5.50,6.90]	6.20[5.60,7.10]	6.50[5.90,7.30]	<0.001	5.80[5.30,6.60]	6.00[5.50,6.80]	0.011
Red blood cell count(millioncells/uL)	5.27[5.14,5.44]	5.27[5.15,5.47]	5.26[5.13,5.44]	0.001	5.08[4.95,5.25]	5.12[4.98,5.35]	0.002
Glycohemoglobin(%)	5.50[5.50,5.60]	6.20[6.10,6.30]	9.60[8.80,10.90]	<0.001	6.80[6.40,7.70]	7.60[6.80,8.60]	<0.001
Mean Cell Hgb Conc.(g/dL)	35.00[34.80,35.30]	34.80[34.60,35.20]	34.80[34.60,35.30]	<0.001	35.00[34.80,35.30]	34.70[34.46,35.10]	<0.001
Red cell distribution width(%)	13.90[13.60,14.50]	14.80[14.30,15.50]	14.90[14.50,15.90]	<0.001	14.30[13.90,15.00]	14.70[14.30,15.30]	<0.001
Mean platelet volume(fL)	9.20[8.90,9.60]	9.30[9.00,9.80]	9.40[9.20,9.90]	<0.001	9.30[9.10,9.60]	9.40[9.30,9.60]	<0.001
Blood lead(umol/L)	0.14[0.12,0.18]	0.15[0.13,0.20]	0.14[0.12,0.18]	<0.001	0.18[0.16,0.23]	0.23[0.20,0.30]	<0.001

Folate,serum(nmol/L)	52.50[44.60,64.10]	62.50[54.20,73.60]	36.60[27.40,52.80]	<0.001	66.60[59.60,76.43]	60.70[50.30,72.86]	0.009
Folate,RBC(nmol/LRBC)	1426.20[1250.00,1720.00]	1620.00[1420.00,1960.00]	1830.00[1570.00,2300.00]	<0.001	901.50[690.80,1680.00]	802.00[573.93,1300.00]	<0.001
Homocysteine(umol/L)	9.66[9.50,9.82]	8.27[6.91,9.86]	8.20[6.71,9.85]	<0.001	8.63[7.33,11.45]	9.11[7.64,14.71]	<0.001
Cotinine,Serum(ng/mL)	216.00[61.12,318.00]	88.27[82.95,92.81]	169.00[35.09,282.52]	<0.001	87.49[0.53,231.00]	192.98[29.47,310.30]	<0.001
gamma-tocopherol(umol/L)	7.57[6.97,8.46]	8.29[7.68,8.94]	8.74[8.26,9.25]	<0.001	8.26[7.62,9.05]	8.85[8.38,9.39]	<0.001
Retinol(umol/L)	2.60[2.43,2.89]	2.69[2.49,2.99]	2.81[2.62,3.24]	<0.001	2.97[2.78,3.31]	2.75[2.62,2.97]	<0.001
Alkaline Phosphatase(ALP)(U/L)	88.00[85.00,93.00]	92.00[89.00,95.00]	95.00[93.00,97.00]	<0.001	91.00[88.00,95.00]	99.00[98.72,99.00]	<0.001
Blood urea nitrogen(mmol/L)	6.43[5.71,7.14]	7.14[6.43,7.85]	7.85[7.50,8.57]	<0.001	7.85[7.14,8.45]	8.20[7.69,8.60]	<0.001
Gamma Glutamyl Transferase(GGT)(U/L)	33.00[9.00,45.00]	43.00[36.00,55.00]	50.00[42.00,63.00]	<0.001	37.00[31.00,47.00]	43.00[36.00,61.61]	<0.001
Iron(umol/L)	21.10[8.60,24.70]	18.40[8.40,21.30]	17.60[8.20,20.60]	<0.001	165.00[157.00,183.00]	177.00[168.00,197.00]	<0.001
Lactate Dehydrogenase(LDH)(U/L)	155.00[98.00,169.00]	169.00[160.00,187.00]	167.00[157.00,181.00]	<0.001	166.00[158.00,184.00]	180.00[169.00,199.00]	<0.001
Uric acid(umol/L)	410.40[386.60,446.10]	440.20[416.40,475.80]	446.10[422.30,487.70]	<0.001	434.20[410.40,469.90]	452.00[428.30,493.70]	<0.001
Creatinine(umol/L)	90.17[88.40,97.24]	97.24[93.70,97.24]	98.61[98.12,99.01]	<0.001	97.24[97.20,98.12]	79.60[67.18,103.43]	<0.001
Potassium(mmol/L)	4.40[4.30,4.51]	4.40[4.30,4.60]	4.53[4.40,4.70]	<0.001	4.50[4.40,4.70]	4.70[4.50,4.80]	<0.001
Globulin(g/L)	34.00[33.00,36.00]	36.00[34.00,38.00]	37.00[36.00,39.00]	<0.001	34.00[33.00,37.00]	38.00[36.00,41.00]	<0.001
trans-lycopene(umol/L)	0.66[0.59,0.76]	0.63[0.56,0.74]	0.58[0.51,0.68]	<0.001	0.58[0.53,0.71]	0.52[0.46,0.63]	0.002
VitaminD(nmol/L)	82.50[77.70,89.60]	76.20[70.60,83.50]	73.00[68.20,80.30]	<0.001	82.50[77.70,89.60]	73.00[71.81,80.10]	<0.001
Direct HDL-Cholesterol(mmol/L)	1.91 [1.78, 2.15]	1.81 [1.68, 2.02]	1.63 [1.53, 1.81]	<0.001	1.80[1.68,2.02]	1.94[1.78,2.15]	0.005

Table 3. Genetically Predicted HDL-C and T2D/MCI Risk

Outcome	**MR method**	**Numbers of SNPs**	***β***	**SE**	**OR (95% CI)**	***P* value for association**	***P* value for heterogeneity test**	***P* value for MR-Egger intercept**	***P* value for MR-PRESSO global test**	**Outlier**
Type 2 diabetes	MR Egger	132	-0.0319	0.0408	0.9686(0.8941,1.0493)	0.4362	1.105E-08	0.0522	<0.0003	NA
	Weighted median		-0.0689	0.0294	0.9334(0.8812,0.9888)	0.0190				
	Inverse variance weighted		-0.0988	0.0226	0.9059(0.8666,0.9470)	0.0000				
	Simple mode		-0.1435	0.0645	0.8663(0.7634,0.9832)	0.0279				

	Weighted mode		-0.0726	0.0292	0.9300(0.8783,0.9847)	0.0141				
	MR Egger		0.0550	0.0202	1.0565(1.0156,1.0991)	0.0072				
	Weighted median		0.0677	0.0189	1.0701(1.0311,1.1105)	0.0003				
Alzheimer's disease	Inverse variance weighted	134	0.0490	0.0127	1.0502(1.0244,1.0767)	0.0001	0.1135	0.7016	0.1363	rs1846692
	Simple mode		0.0334	0.0337	1.0339(0.9678,1.1045)	0.3238				
	Weighted mode		0.0564	0.0159	1.0580(1.0255,1.0915)	0.0006				

503

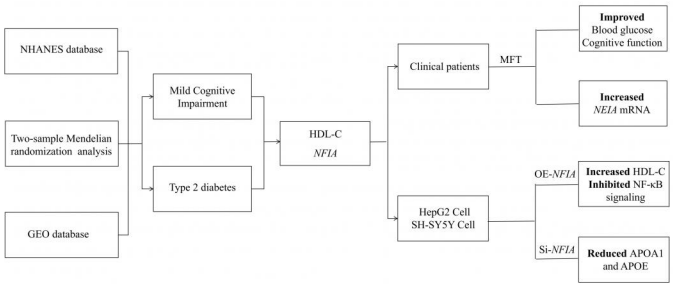

NHANES database
Two-sample Mendelian randomization analysis
GEO database
Mild Cognitive Impairment
Type 2 diabetes
HDL-C
NFIA
Clinical patients
MFT
Improved
Blood glucose
Cognitive function
Increased
NEIA mRNA
HepG2 Cell
SH-SY5Y Cell
OE-NFIA
Increased HDL-C
Inhibited NF-κB
signaling
Si-NFIA
Reduced APOA1
and APOE

Table 1. Demographic and individual characteristics

		Normal	Prediabetes	T2D	p	Normal	MCI	p
		n=32586,66.40%	n=10136,20.65%	n=6356,12.95%		n=3873,77.30%	n=1138,22.70%	
GENDER, n(%)	Female	17042(51.5)	5049(52.2)	3076(48.2)	<0.001	2027(55.1)	512(54.1)	0.67
	Male	15544(48.5)	5087(47.8)	3280(51.8)		1846(44.9)	626(45.9)	
T2D (%)	normal	—	—	—	—	1859(51.9)	428(41.3)	<0.001
	prediabetes	—	—	—		1218(30.7)	364(29.2)	
	type 2 diabetes	—	—	—		796(17.5)	346(29.5)	
AGE, mean(SD)		41.78(16.17)	55.67(15.38)	58.86(13.83)	<0.001	69.01(6.69)	73.19(7.38)	<0.001
Race/Ethnicity, n(%)	Mexican American	6165(8.2)	1702(8.5)	1333(9.5)	<0.001	414(2.3)	299(9.0)	<0.001
	Other Hispanic	2522(5.5)	905(5.7)	598(6.1)		215(2.7)	157(13.2)	
	Non-Hispanic White	15318(71.2)	3849(62.4)	2166(60.5)		2341(85.3)	333(55.6)	
	Non-Hispanic Black	5769(8.8)	2706(15.6)	1635(15.0)		634(5.6)	306(18.4)	
	Other	2812(6.3)	974(7.7)	624(8.9)		269(4.1)	43(3.9)	
Education level, n(%)	<high school	8085(15.5)	3075(21.1)	2358(25.5)	<0.001	802(15.3)	787(59.1)	<0.001
	>high school	16655(60.7)	4554(51.9)	2571(49.5)		2072(59.0)	152(18.2)	
	high school	7819(23.7)	2496(26.9)	1418(25.0)		997(25.7)	194(22.3)	
	others	27(0.1)	10(0.1)	9(0.1)		2(0.0)	4(0.4)	
	NA	0(0.0)	1(0.0)	0.0(0.0)		0(0.0)	1(0.0)	
Hypertention, n(%)	normal	20645(63.1)	3419(35.9)	1080(17.9)	<0.001	773(21.4)	155(13.4)	<0.001
	hypertention	11941(36.9)	6717(64.1)	5276(82.1)		3100(78.6)	983(86.6)	
Obesity/Overweight, n(%)	normal	10121(30.3)	1534(14.9)	580(8.0)	<0.001	774(20.3)	228(22.2)	0.472
	overweight	13400(41.6)	4079(39.1)	2124(29.2)		45.5(44.4)	521(45.3)	
	obesity	9065(28.1)	4523(46.0)	3652(62.8)		34.5(35.2)	389(32.5)	
Central obesity, n(%)	normal	17812(54.0)	3321(30.1)	1343(17.6)	<0.001	1377(32.6)	417(33.6)	0.628
	central obesity	14774(46.0)	6815(69.9)	5013(82.4)		2496(67.4)	721(66.4)	
SBP(mmHg)		116.70[108.70,127.30]	125.30[115.30,137.30]	128.00[117.30,141.00]	<0.001	131.30[120.00,145.30]	139.30[126.00,155.86]	<0.001

DBP(mmHg)	70.70[64.00,78.00]	72.70[64.70,79.30]	70.70[62.00,78.00]	<0.001	70.70[62.70,77.30]	67.30[59.30,76.00]	<0.001
BMI(kg/m^2)	26.59[23.30,30.65]	29.30[25.76,34.00]	31.80[27.90,37.14]	<0.001	27.81[24.63,31.60]	27.60[24.20,31.53]	0.237
Waist Circumference (cm)	93.50[83.60,104.20]	102.40[93.20,112.30]	110.30[100.00,121.50]	<0.001	100.60[91.50,109.77]	100.10[91.50,109.50]	0.646
HbA1c (%)	5.20[5.00,5.40]	5.80[5.70,6.00]	7.00[6.40,8.10]	<0.001	5.60[5.40,6.00]	5.80[5.40,6.40]	<0.001

Table 2. Importent common differential laboratory characteristics

Terms	Normal	Prediabetes	T2D	p	Normal	MCI	p
Albumin,urine(ug/mL)	6.70[4.20,15.20]	6.90[4.40,19.90]	8.30[6.40,57.67]	<0.001	6.50[4.10,21.80]	8.90[6.00,53.81]	<0.001
Creatinine,urine(mg/dL)	80.00[49.00,207.00]	80.00[49.00,192.00]	83.00[52.00,172.00]	0.009	74.00[43.00,156.00]	80.00[50.00,175.00]	0.006
White blood cell count(1000cells/uL)	9.50[8.90,10.60]	9.80[9.10,11.00]	10.20[9.40,11.40]	<0.001	8.75[8.40,9.20]	9.10[8.60,9.44]	<0.001
Lymphocyte percent(%)	39.60[37.40,43.10]	40.80[38.20,44.90]	39.30[36.80,43.30]	<0.001	38.10[35.70,41.70]	39.20[36.58,43.53]	0.008
Lymphocyte number(1000cells/uL)	2.90[2.70,3.30]	3.10[2.80,3.50]	3.20[2.90,3.60]	<0.001	2.70[2.50,3.10]	2.90[2.60,3.30]	<0.001
Segmented neutrophils number(1000cells/uL)	6.10[5.50,6.90]	6.20[5.60,7.10]	6.50[5.90,7.30]	<0.001	5.80[5.30,6.60]	6.00[5.50,6.80]	0.011
Red blood cell count(millioncells/uL)	5.27[5.14,5.44]	5.27[5.15,5.47]	5.26[5.13,5.44]	0.001	5.08[4.95,5.25]	5.12[4.98,5.35]	0.002
Glycohemoglobin(%)	5.50[5.50,5.60]	6.20[6.10,6.30]	9.60[8.80,10.90]	<0.001	6.80[6.40,7.70]	7.60[6.80,8.60]	<0.001
Mean Cell Hgb Conc.(g/dL)	35.00[34.80,35.30]	34.80[34.60,35.20]	34.80[34.60,35.30]	<0.001	35.00[34.80,35.30]	34.70[34.46,35.10]	<0.001
Red cell distribution width(%)	13.90[13.60,14.50]	14.80[14.30,15.50]	14.90[14.50,15.90]	<0.001	14.30[13.90,15.00]	14.70[14.30,15.30]	<0.001
Mean platelet volume(fL)	9.20[8.90,9.60]	9.30[9.00,9.80]	9.40[9.20,9.90]	<0.001	9.30[9.10,9.60]	9.40[9.30,9.60]	<0.001
Blood lead(umol/L)	0.14[0.12,0.18]	0.15[0.13,0.20]	0.14[0.12,0.18]	<0.001	0.18[0.16,0.23]	0.23[0.20,0.30]	<0.001
Folate,serum(nmol/L)	52.50[44.60,64.10]	62.50[54.20,73.60]	36.60[27.40,52.80]	<0.001	66.60[59.60,76.43]	60.70[50.30,72.86]	0.009
Folate,RBC(nmol/LRBC)	1426.20[1250.00,1720.00]	1620.00[1420.00,1960.00]	1830.00[1570.00,2300.00]	<0.001	901.50[690.80,1680.00]	802.00[573.93,1300.00]	<0.001
Homocysteine(umol/L)	9.66[9.50,9.82]	8.27[6.91,9.86]	8.20[6.71,9.85]	<0.001	8.63[7.33,11.45]	9.11[7.64,14.71]	<0.001
Cotinine,Serum(ng/mL)	216.00[61.12,318.00]	88.27[82.95,92.81]	169.00[35.09,282.52]	<0.001	87.49[0.53,231.00]	192.98[29.47,310.30]	<0.001
gamma-tocopherol(umol/L)	7.57[6.97,8.46]	8.29[7.68,8.94]	8.74[8.26,9.25]	<0.001	8.26[7.62,9.05]	8.85[8.38,9.39]	<0.001
Retinol(umol/L)	2.60[2.43,2.89]	2.69[2.49,2.99]	2.81[2.62,3.24]	<0.001	2.97[2.78,3.31]	2.75[2.62,2.97]	<0.001
Alkaline Phosphatase(ALP)(U/L)	88.00[85.00,93.00]	92.00[89.00,95.00]	95.00[93.00,97.00]	<0.001	91.00[88.00,95.00]	99.00[98.72,99.00]	<0.001
Blood urea nitrogen(mmol/L)	6.43[5.71,7.14]	7.14[6.43,7.85]	7.85[7.50,8.57]	<0.001	7.85[7.14,8.45]	8.20[7.69,8.60]	<0.001
Gamma Glutamyl Transferase(GGT)(U/L)	33.00[9.00,45.00]	43.00[36.00,55.00]	50.00[42.00,63.00]	<0.001	37.00[31.00,47.00]	43.00[36.00,61.61]	<0.001
Iron(umol/L)	21.10[8.60,24.70]	18.40[8.40,21.30]	17.60[8.20,20.60]	<0.001	165.00[157.00,183.00]	177.00[168.00,197.00]	<0.001
Lactate Dehydrogenase(LDH)(U/L)	155.00[98.00,169.00]	169.00[160.00,187.00]	167.00[157.00,181.00]	<0.001	166.00[158.00,184.00]	180.00[169.00,199.00]	<0.001
Uric acid(umol/L)	410.40[386.60,446.10]	440.20[416.40,475.80]	446.10[422.30,487.70]	<0.001	434.20[410.40,469.90]	452.00[428.30,493.70]	<0.001
Creatinine(umol/L)	90.17[88.40,97.24]	97.24[93.70,97.24]	98.61[98.12,99.01]	<0.001	97.24[97.20,98.12]	79.60[67.18,103.43]	<0.001

Potassium(mmol/L)	4.40[4.30,4.51]	4.40[4.30,4.60]	4.53[4.40,4.70]	<0.001	4.50[4.40,4.70]	4.70[4.50,4.80]	<0.001
Globulin(g/L)	34.00[33.00,36.00]	36.00[34.00,38.00]	37.00[36.00,39.00]	<0.001	34.00[33.00,37.00]	38.00[36.00,41.00]	<0.001
trans-lycopene(umol/L)	0.66[0.59,0.76]	0.63[0.56,0.74]	0.58[0.51,0.68]	<0.001	0.58[0.53,0.71]	0.52[0.46,0.63]	0.002
VitaminD(nmol/L)	82.50[77.70,89.60]	76.20[70.60,83.50]	73.00[68.20,80.30]	<0.001	82.50[77.70,89.60]	73.00[71.81,80.10]	<0.001
Direct HDL-Cholesterol(mmol/L)	1.91 [1.78, 2.15]	1.81 [1.68, 2.02]	1.63 [1.53, 1.81]	<0.001	1.80[1.68,2.02]	1.94[1.78,2.15]	0.005

Table 3. Genetically Predicted HDL-C and T2D/MCI Risk

Outcome	MR method	Numbers of SNPs	*β*	SE	OR (95% CI)	*P* value for association	*P* value for heterogeneity test	*P* value for MR-Egger intercept	*P* value for MR-PRESSO global test	Outlier
Type 2 diabetes	MR Egger	132	-0.0319	0.0408	0.9686(0.8941,1.0493)	0.4362	1.105E-08	0.0522	<0.0003	NA
	Weighted median		-0.0689	0.0294	0.9334(0.8812,0.9888)	0.0190				
	Inverse variance weighted		-0.0988	0.0226	0.9059(0.8666,0.9470)	0.0000				
	Simple mode		-0.1435	0.0645	0.8663(0.7634,0.9832)	0.0279				
	Weighted mode		-0.0726	0.0292	0.9300(0.8783,0.9847)	0.0141				
Alzheimer's disease	MR Egger	134	0.0550	0.0202	1.0565(1.0156,1.0991)	0.0072	0.1135	0.7016	0.1363	rs1846692
	Weighted median		0.0677	0.0189	1.0701(1.0311,1.1105)	0.0003				
	Inverse variance weighted		0.0490	0.0127	1.0502(1.0244,1.0767)	0.0001				
	Simple mode		0.0334	0.0337	1.0339(0.9678,1.1045)	0.3238				
	Weighted mode		0.0564	0.0159	1.0580(1.0255,1.0915)	0.0006				

Supplementary Table 1. Characteristics of GWAS enrolled in the MR study

Items	Dataset	Sample size	p-value for screening	No. of enrolled SNPs
Type 2 diabetes	GCST90018926	667504	——	24024799
Alzheimer's disease	GCST005922	388324	——	7561814
Red cell distribution width	GCST90078986	534313	<5.00E-2	33
Folate	GCST90013344	5944	<5.00E-6	14
Gamma-tocopherol	GCST90243688	6226	<5.00E-5	69
Alkaline Phosphatase	GCST90018942	463178	<5.00E-15	150
Blood urea nitrogen	GCST008062	416178	<5.00E-8	146
Gamma Glutamyl Transferase	GCST90019507	355690	<5.00E-23	142
Uric acid	GCST90018977	473241	<5.00E-23	147
Creatinine	GCST90278624	92615	<5.00E-8	92
Globulin	GCST90101080	1335	<5.00E-7	10
Vitamin D	GCST90019526	339705	<5.00E-8	119
HDL-Cholesterol	GCST007140	94675	<5.00E-8	176

Supplementary Table 2. Primer sequences used in this study.

Primer name	Primer Sequence (5' to 3')
GAPDH-Forward	ACAACTTTGGTATCGTGGAAGG
GAPDH-Reverse	GCCATCACGCCACAGTTTC
NFIA-Forward	GCAGGCCCGAAAACGAAAATA
NFIA-Reverse	TTTGCCAGAAGTCGAGATGCC
APOA1-Forward	CCCTGGGATCGAGTGAAGGA
APOA1-Reverse	CTGGGACACATAGTCTCTGCC
APOE-Forward	GTTGCTGGTCACATTCCTGG
APOE-F-Reverse	GCAGGTAATCCCAAAAGCGAC

Supplementary Table 3. Quartile and comparison of laboratory characteristics between different groups

Terms	Normal	Prediabetes	T2D	p	Normal	MCI	p
White blood cell count (1000 cells/uL)	6.90[5.60,8.20]	7.20[6.00,8.60]	7.60[6.30,9.10]	<0.001	6.70[5.60,8.00]	6.90[5.80,8.18]	0.015
Lymphocyte percent（%）	29.80[24.80,35.10]	30.10[24.90,35.50]	28.30[22.90,34.00]	<0.001	27.80[22.80,33.40]	27.00[21.40,33.70]	0.15
Segmented neutrophils percent（%）	58.70[52.70,64.40]	58.20[52.00,64.00]	60.20[53.90,65.90]	<0.001	60.10[53.80,65.60]	60.90[53.80,66.69]	0.153
Eosinophils percent（%）	2.30[1.50,3.40]	2.50[1.60,3.70]	2.50[1.70,3.60]	<0.001	2.50[1.70,3.70]	2.50[1.60,3.70]	0.555
Basophils percent（%）	0.60[0.40,0.90]	0.70[0.40,0.90]	0.70[0.50,0.90]	<0.001	0.60[0.40,0.90]	0.60[0.40,0.80]	<0.001
Lymphocyte number (1000 cells/uL)	2.00[1.60,2.50]	2.10[1.70,2.60]	2.10[1.70,2.60]	<0.001	1.80[1.50,2.30]	1.80[1.40,2.30]	0.673
Monocyte number (1000 cells/uL)	0.50[0.40,0.60]	0.60[0.50,0.70]	0.60[0.50,0.70]	<0.001	0.50[0.40,0.70]	0.60[0.50,0.70]	0.036
Segmented neutrophils num (1000 cells/uL)	4.00[3.10,5.10]	4.10[3.20,5.30]	4.50[3.60,5.60]	<0.001	4.00[3.20,4.90]	4.18[3.20,5.20]	0.009
Eosinophils number (1000 cells/uL)	0.20[0.10,0.20]	0.20[0.10,0.30]	0.20[0.10,0.30]	<0.001	0.20[0.10,0.30]	0.20[0.10,0.30]	0.444
Basophils number (1000 cells/uL)	0.00[0.00,0.10]	0.00[0.00,0.10]	0.10[0.00,0.10]	<0.001	0.00[0.00,0.10]	0.00[0.00,0.10]	0.002
Red blood cell count (million cells/uL)	4.70[4.37,5.05]	4.71[4.40,5.04]	4.70[4.35,5.04]	0.114	4.55[4.27,4.84]	4.51[4.14,4.86]	0.055
Hemoglobin (g/dL)	14.40[13.50,15.40]	14.20[13.30,15.10]	14.10[13.10,15.10]	<0.001	14.10[13.30,15.00]	13.80[12.60,14.90]	<0.001
Hematocrit (%)	42.40[39.30,45.30]	42.00[39.10,44.90]	41.60[38.30,44.40]	<0.001	41.60[39.10,44.30]	41.10[37.80,44.20]	0.037
Mean cell volume (fL)	90.20[87.30,93.10]	89.60[86.10,92.60]	89.10[85.80,92.20]	<0.001	91.70[88.90,94.40]	91.30[87.70,94.70]	0.096
Mean cell hemoglobin (pg)	30.80[29.60,31.80]	30.30[29.00,31.50]	30.20[28.90,31.40]	<0.001	31.30[30.10,32.30]	30.80[29.40,32.30]	<0.001
Mean Cell Hgb Conc. (g/dL)	34.00[33.50,34.60]	33.80[33.20,34.30]	33.80[33.20,34.40]	<0.001	34.00[33.40,34.60]	33.70[33.10,34.30]	<0.001
Red cell distribution width (%)	12.60[12.20,13.30]	13.10[12.60,13.90]	13.20[12.50,14.00]	<0.001	13.00[12.50,13.60]	13.20[12.60,14.00]	<0.001
Platelet count (1000 cells/uL)	247.00[211.00,289.00]	250.00[210.00,296.00]	238.00[200.00,290.00]	<0.001	231.00[195.00,273.00]	230.00[190.00,278.00]	0.57
Mean platelet volume (fL)	8.10[7.60,8.70]	8.10[7.60,8.70]	8.20[7.60,8.90]	<0.001	8.20[7.60,8.90]	8.40[7.70,9.00]	0.101
Blood lead (umol/L)	0.06[0.04,0.10]	0.07[0.05,0.11]	0.06[0.04,0.09]	<0.001	0.09[0.06,0.13]	0.10[0.07,0.16]	0.17
Folate, RBC (nmol/L RBC)	829.00[591.20,1160.00]	955.00[668.00,1340.82]	1037.13[727.10,1467.53]	<0.001	1060.00[762.00,1520.00]	865.33[600.73,1250.81]	<0.001
Folate, serum (nmol/L)	29.70[20.70,42.40]	32.60[21.90,49.50]	33.80[23.60,51.50]	<0.001	40.30[27.40,57.10]	33.50[22.70,49.04]	0.014
Vitamin B12 (pmol/L)	346.90[264.20,461.08]	363.13[267.89,486.30]	362.40[268.28,512.91]	<0.001	378.25[275.91,528.40]	363.71[257.57,526.20]	0.229
Homocysteine(umol/L)	7.70[6.36,9.33]	8.52[7.01,10.47]	8.75[7.04,10.95]	<0.001	9.07[7.51,11.09]	10.53[8.00,13.39]	<0.001

Blood mercury, total (nmol/L)	4.49[2.30,8.98]	4.60[2.40,9.08]	3.99[2.15,8.08]	0.001	5.00[2.70,10.80]	3.60[1.70,7.50]	0.012
Mercury, inorganic (nmol/L)	1.25[1.25,1.50]	1.25[0.95,1.50]	1.25[0.95,1.50]	<0.001	0.95[0.95,1.70]	0.95[0.95,0.95]	0.014
Tot Iron Binding Capacity TIBC (umol/L)	62.65[56.21,70.17]	61.07[55.31,67.66]	61.58[54.98,68.60]	<0.001	63.90[57.28,70.47]	62.65[55.85,69.81]	0.245
Ferritin(ug/L)	65.00[30.09,129.00]	91.64[43.00,169.00]	107.00[50.00,210.00]	<0.001	104.00[55.00,186.00]	110.00[57.00,195.91]	0.439
Cotinine, Serum (ng/mL)	0.06[0.02,23.20]	0.04[0.01,24.53]	0.04[0.01,0.76]	<0.001	0.03[0.01,0.11]	0.04[0.02,0.54]	<0.001
gamma-tocopherol (umol/L)	4.64[3.05,6.46]	5.07[3.29,7.37]	5.38[3.44,7.90]	<0.001	4.35[2.33,7.06]	4.71[2.89,7.73]	0.032
Retinyl palmitate (umol/L)	0.05[0.03,0.09]	0.05[0.03,0.08]	0.05[0.03,0.09]	0.002	0.07[0.04,0.11]	0.05[0.03,0.08]	<0.001
Retinyl stearate (umol/L)	0.02[0.01,0.02]	0.02[0.01,0.02]	0.02[0.01,0.02]	<0.001	0.01[0.01,0.02]	0.01[0.01,0.02]	0.966
Retinol (umol/L)	1.98[1.63,2.38]	1.98[1.64,2.39]	2.07[1.69,2.52]	<0.001	2.28[1.95,2.68]	2.14[1.76,2.58]	<0.001
Albumin, urine (ug/mL)	6.70[3.50,12.60]	7.80[4.10,15.90]	12.40[5.50,35.56]	<0.001	7.80[3.83,17.00]	15.40[6.40,38.58]	<0.001
Albumin (g/L)	43.00[41.00,46.00]	42.00[40.00,44.00]	42.00[39.00,44.00]	<0.001	43.00[41.00,44.00]	42.00[40.00,44.00]	<0.001
Creatinine, urine (mg/dL)	113.00[61.00,174.00]	109.00[61.00,164.00]	104.00[64.00,154.00]	<0.001	92.00[50.00,140.00]	100.00[58.00,152.00]	0.006
Creatinine (umol/L)	72.49[61.88,87.52]	76.91[64.53,88.40]	76.91[61.90,92.82]	<0.001	79.56[64.53,92.82]	79.60[67.18,102.54]	0.004
Alanine Aminotransferase (ALT) (U/L)	20.00[16.00,28.00]	22.00[17.00,30.00]	23.00[17.00,31.00]	<0.001	20.00[17.00,25.00]	19.00[15.00,24.00]	<0.001
Aspartate Aminotransferase (AST) (U/L)	22.00[19.00,27.00]	23.00[20.00,28.00]	22.00[19.00,28.00]	<0.001	23.00[20.00,27.00]	23.00[20.00,27.00]	0.811
Alkaline Phosphatase (ALP) (U/L)	65.00[53.00,79.00]	70.00[57.00,84.00]	71.00[57.00,88.00]	<0.001	67.00[55.00,81.00]	76.00[61.00,94.39]	<0.001
Blood urea nitrogen (mmol/L)	4.28[3.57,5.36]	5.00[3.93,6.07]	5.36[3.93,6.78]	<0.001	5.36[4.30,6.78]	5.71[4.60,7.29]	0.001
Total Calcium (mmol/L)	2.35[2.30,2.42]	2.35[2.30,2.40]	2.35[2.30,2.42]	0.001	2.35[2.30,2.42]	2.38[2.30,2.42]	0.442
Bicarbonate (mmol/L)	25.00[23.00,26.00]	25.00[24.00,27.00]	25.00[23.00,26.00]	<0.001	25.00[24.00,27.00]	25.00[23.00,26.00]	0.011
Gamma Glutamyl Transferase (GGT) (U/L)	18.00[13.00,28.00]	22.00[16.00,33.00]	24.00[17.00,39.00]	<0.001	19.00[15.00,27.22]	21.00[15.00,33.00]	<0.001
Iron (umol/L)	15.40[11.60,20.06]	14.10[10.70,18.10]	13.40[10.40,17.20]	<0.001	15.00[11.64,18.81]	13.61[10.57,17.73]	<0.001
Lactate Dehydrogenase (LDH) (U/L)	127.00[112.00,144.00]	136.00[120.00,156.00]	133.36[117.00,155.00]	<0.001	134.00[119.00,152.00]	143.00[125.00,166.00]	<0.001
Phosphorus (mmol/L)	1.20[1.10,1.32]	1.20[1.07,1.32]	1.20[1.07,1.32]	0.328	1.16[1.07,1.29]	1.16[1.03,1.29]	0.063
Bilirubin, total (umol/L)	10.30[8.55,13.68]	10.26[6.84,13.68]	10.26[6.84,13.68]	<0.001	10.30[8.55,13.68]	10.26[8.55,13.68]	0.222
Protein, total (g/L)	72.00[69.00,75.00]	71.00[68.00,74.00]	71.00[68.00,74.00]	<0.001	71.00[68.00,74.00]	73.00[69.00,77.00]	<0.001
Uric acid (umol/L)	309.30[255.80,368.80]	333.10[279.60,386.60]	327.10[273.60,398.50]	<0.001	327.10[273.60,386.60]	333.10[273.60,400.86]	0.037

Sodium (mmol/L)	139.00[138.00,141.00]	139.00[138.00,141.00]	139.00[137.00,141.00]	<0.001	140.00[138.00,141.00]	140.00[138.00,141.00]	0.972
Potassium (mmol/L)	4.00[3.80,4.20]	4.00[3.80,4.27]	4.10[3.83,4.30]	<0.001	4.10[3.90,4.30]	4.10[3.90,4.40]	0.03
Chloride (mmol/L)	104.00[102.00,105.00]	103.00[101.00,105.00]	102.00[100.00,104.00]	<0.001	103.00[101.00,105.00]	103.00[100.30,105.00]	0.008
Transferrin Saturation (%)	24.70[18.00,32.80]	23.24[17.60,30.00]	23.00[17.00,29.00]	<0.001	24.00[18.30,30.60]	22.50[16.44,29.15]	0.118
Globulin (g/L)	28.00[26.00,31.00]	29.00[26.00,32.00]	30.00[27.00,33.00]	<0.001	28.00[25.00,31.00]	31.00[28.00,34.00]	<0.001
alpha-carotene (umol/L)	0.05[0.03,0.10]	0.05[0.03,0.09]	0.04[0.02,0.08]	<0.001	0.06[0.04,0.11]	0.05[0.02,0.09]	0.004
trans-beta-carotene (umol/L)	0.23[0.13,0.42]	0.23[0.13,0.41]	0.18[0.10,0.34]	<0.001	0.34[0.20,0.56]	0.31[0.17,0.54]	0.163
cis-beta-carotene (umol/L)	0.01[0.01,0.02]	0.01[0.01,0.02]	0.01[0.01,0.02]	<0.001	0.02[0.01,0.03]	0.02[0.01,0.03]	0.711
beta-cryptoxanthin (umol/L)	0.13[0.08,0.20]	0.12[0.07,0.20]	0.10[0.06,0.17]	<0.001	0.15[0.09,0.24]	0.14[0.08,0.24]	0.211
Lutein and zeaxanthin (umol/L)	0.25[0.18,0.36]	0.27[0.19,0.38]	0.26[0.18,0.36]	0.004	0.28[0.20,0.39]	0.26[0.19,0.38]	0.317
trans-lycopene (umol/L)	0.42[0.30,0.56]	0.37[0.25,0.54]	0.34[0.22,0.49]	<0.001	0.34[0.22,0.49]	0.30[0.20,0.41]	0.035
Vitamin D (nmol/L)	63.10[49.20,77.70]	55.70[42.00,68.20]	53.20[39.80,68.24]	<0.001	61.10[49.20,73.00]	56.30[42.00,70.60]	0.02
Creatine Phosphokinase (CPK) (IU/L)	104.00[73.00,162.00]	114.00[78.00,178.00]	100.00[66.00,154.00]	<0.001	96.00[67.00,138.00]	95.00[66.00,158.00]	0.694
Direct HDL-Cholesterol (mmol/L)	1.60[1.29,2.01]	1.42[1.27,1.71]	1.19[1.06,1.34]	<0.001	1.29[1.08,1.58]	1.37[1.14,1.71]	0.014
Direct HDL-Cholesterol (mg/dL)	52.00[43.00,63.00]	49.00[41.00,59.00]	45.00[38.00,54.00]	<0.001	52.00[43.00,65.00]	49.00[41.00,61.00]	0.001
Total Cholesterol(mmol/L)	4.94[4.29,5.66]	5.20[4.53,5.92]	4.73[4.01,5.56]	<0.001	5.20[4.50,5.90]	5.12[4.32,5.97]	0.486
Cholesterol, total (mmol/L)	4.96[4.32,5.66]	5.20[4.50,5.90]	4.73[4.01,5.56]	<0.001	5.15[4.42,5.82]	5.07[4.29,5.90]	0.277
Triglyceride (mg/dL)	97.00[67.00,143.00]	116.00[83.00,169.00]	141.68[96.00,204.00]	<0.001	117.00[81.00,165.00]	120.00[83.00,170.00]	0.708
Triglyceride (mmol/L)	1.09[0.76,1.61]	1.31[0.94,1.91]	1.60[1.08,2.30]	<0.001	1.32[0.91,1.86]	1.35[0.94,1.92]	0.707
LDL-cholesterol(mmol/L)	2.90[2.35,3.52]	3.08[2.48,3.70]	2.59[2.02,3.28]	<0.001	2.87[2.28,3.60]	3.00[2.40,3.59]	0.197
Glycohemoglobin(%)	5.20[5.00,5.40]	5.80[5.70,6.00]	6.90[6.30,7.90]	<0.001	5.60[5.40,6.00]	5.80[5.40,6.40]	<0.001
Glucose, serum (mmol/L)	4.94[4.61,5.27]	5.38[4.94,5.88]	7.16[5.77,9.71]	<0.001	5.33[4.94,6.00]	5.55[5.05,6.49]	<0.001
Glucose, plasma (mg/dL)	95.76[89.90,102.00]	105.00[98.00,113.00]	142.19[119.00,181.00]	<0.001	106.55[96.00,124.73]	103.20[95.70,114.00]	0.011
Plasma glucose: SI(mmol/L)	5.32[4.99,5.66]	5.83[5.44,6.27]	7.89[6.61,10.05]	<0.001	5.92[5.33,6.93]	5.73[5.32,6.33]	0.011
C-peptide:SI(nmol/L)	0.66[0.50,0.90]	0.98[0.75,1.30]	1.06[0.78,1.42]	<0.001	0.94[0.63,1.25]	0.82[0.61,1.10]	0.048
Insulin(uU/mL)	8.24[5.47,12.75]	11.78[7.29,18.58]	14.07[8.59,23.56]	<0.001	11.26[6.92,16.45]	10.01[6.47,15.40]	0.04

Insulin:SI(pmol/L)	53.28[38.58,74.81]	83.25[54.51,119.58]	109.51[64.65,159.47]	<0.001	71.64[45.19,108.95]	60.06[42.65,89.72]	0.046
Two Hour Glucose(OGTT)(mg/dL)	99.00[82.00,121.00]	125.00[100.00,160.00]	272.00[200.00,322.37]	<0.001	141.05[112.70,192.22]	119.00[96.00,156.00]	<0.001

Supplementary Table 4. Comparison of the upper quartile of laboratory characteristics

Terms	Normal	Prediabetes	T2D	p	Normal	MCI	p
Segmented neutrophils percent(%)	68.80[66.60,72.10]	67.80[65.60,71.10]	69.30[67.10,72.60]	<0.001	69.20[67.10,73.10]	69.30[67.20,72.70]	0.78
Eosinophils percent(%)	4.90[4.20,6.00]	4.80[4.20,6.10]	4.90[4.20,6.00]	0.863	4.80[4.20,5.90]	4.90[4.37,6.30]	0.123
Basophils percent(%)	1.20[1.00,1.40]	1.20[1.00,1.40]	1.20[1.00,1.39]	0.381	1.20[1.00,1.40]	1.20[1.00,1.40]	0.732
Monocyte number(1000cells/uL)	0.80[0.70,0.80]	0.90[0.80,1.00]	0.90[0.80,1.00]	<0.001	0.88[0.80,0.90]	0.90[0.80,1.00]	0.191
Eosinophils number(1000 cells/uL)	0.30[0.30,0.40]	0.50[0.40,0.60]	0.50[0.40,0.60]	<0.001	——	——	——
Basophils number(1000 cells/uL)	0.20[0.20,0.20]	0.20[0.20,0.20]	0.20[0.20,0.30]	0.209	——	——	——
Hemoglobin (g/dL)	16.00[15.80,16.50]	15.80[15.40,16.30]	15.60[15.20,16.20]	<0.001	15.60[15.20,16.10]	15.60[15.10,16.00]	0.228
Hematocrit (%)	47.10[46.10,48.50]	46.50[45.60,47.90]	46.30[45.30,47.90]	<0.001	46.20[45.30,47.70]	46.30[45.39,47.70]	0.299
Mean cell volume(fL)	95.20[94.00,96.90]	94.60[93.40,96.40]	94.60[93.40,96.50]	<0.001	96.30[95.40,97.60]	96.10[95.10,97.52]	0.093
Mean cell hemoglobin(pg)	32.70[32.20,33.30]	32.30[31.80,33.00]	32.30[31.80,33.10]	<0.001	33.10[32.70,33.70]	33.00[32.50,33.90]	0.301
Platelet count(1000cells/uL)	325.00[305.00,356.00]	331.00[309.00,365.00]	327.00[305.59,365.00]	<0.001	311.00[288.00,343.00]	312.43[293.00,351.00]	0.351
Vitamin B12(pmol/L)	560.88[507.01,656.10]	605.33[543.20,718.07]	637.63[574.90,738.00]	<0.001	660.05[584.89,752.00]	655.25[580.88,774.89]	0.878
Blood mercury, total(nmol/L)	9.20[8.70,9.60]	9.50[9.30,9.80]	8.98[8.50,9.53]	<0.001	5.70[3.40,13.08]	8.79[8.62,8.80]	0.002
Mercury, inorganic(nmol/L)	10.94(11.92)	14.23(18.53)	10.34(10.51)	0.077	2.54[2.05,3.29]	2.24[1.87,2.95]	0.085
Tot Iron Binding Capacity TIBC(umol/L)	77.69[74.29,82.70]	73.72[70.35,78.04]	73.42[70.71,79.00]	<0.001	75.36[72.14,80.73]	73.83[70.88,78.79]	0.158
Ferritin(ug/L)	62.00[31.00,140.00]	71.93[40.00,207.71]	77.00[44.71,283.50]	<0.001	77.00[47.00,236.00]	75.72[52.00,257.36]	0.703
Retinyl palmitate (umol/L)	0.13[0.10,0.16]	0.12[0.09,0.15]	0.13[0.11,0.19]	<0.001	0.15[0.13,0.20]	0.14[0.10,0.17]	0.006
Retinyl stearate (umol/L)	0.03[0.02,0.04]	0.03[0.03,0.05]	0.04[0.03,0.06]	<0.001	0.04[0.02,0.06]	0.04[0.03,0.05]	0.326
Albumin (g/L)	47.00[46.00,48.00]	46.00[45.00,47.00]	46.00[45.00,47.00]	<0.001	46.00[45.00,47.00]	46.00[45.00,46.00]	0.582
Alanine Aminotransferase (ALT) (U/L)	35.00[30.00,44.00]	37.00[32.00,45.00]	38.00[33.00,49.00]	<0.001	30.00[27.00,36.00]	31.00[27.00,39.00]	0.711
Aspartate Aminotransferase (AST) (U/L)	32.00[29.00,38.00]	33.00[30.00,40.00]	35.00[31.00,44.00]	<0.001	31.00[29.00,35.00]	32.00[29.00,38.03]	0.355
Total Calcium (mmol/L)	2.48[2.45,2.50]	2.45[2.42,2.50]	2.48[2.45,2.52]	<0.001	2.48[2.45,2.52]	2.48[2.45,2.52]	0.445
Bicarbonate (mmol/L)	27.00[27.00,28.00]	28.00[28.00,29.00]	28.00[28.00,29.00]	<0.001	28.00[28.00,29.00]	28.00[27.00,29.00]	<0.001
Phosphorus (mmol/L)	1.42[1.39,1.49]	1.42[1.39,1.49]	1.42[1.39,1.52]	0.031	1.42[1.36,1.45]	1.39[1.32,1.49]	0.002

Bilirubin,total(umol/L)	8.55[6.84,17.10]	8.55[6.80,15.39]	8.55[6.84,15.39]	<0.001	8.55[6.84,15.40]	8.55[6.84,15.39]	0.404
Protein,total(g/L)	78.00[76.00,79.00]	78.00[76.00,80.00]	78.00[77.00,80.00]	0.052	78.00[77.00,80.00]	80.00[79.00,82.00]	<0.001
Sodium(mmol/L)	142.00[142.00,143.00]	142.00[142.00,143.00]	143.00[142.00,143.30]	0.003	142.00[142.00,143.00]	143.00[142.00,143.80]	0.002
Chloride(mmol/L)	106.00[99.50,107.00]	106.00[99.00,107.00]	105.00[98.00,106.00]	<0.001	106.00[99.00,107.00]	105.88[98.00,107.00]	0.031
Transferrin Saturation (%)	37.20[33.30,43.30]	35.00[31.00,39.37]	34.00[30.00,39.00]	<0.001	35.35[32.19,40.46]	33.98[31.30,39.86]	0.229
alpha-carotene(umol/L)	0.16[0.12,0.24]	0.15[0.12,0.24]	0.13[0.11,0.18]	<0.001	0.16[0.13,0.22]	0.16[0.12,0.22]	0.179
trans-beta-carotene(umol/L)	0.63[0.49,0.94]	0.65[0.52,0.91]	0.55[0.44,0.82]	<0.001	0.79[0.64,1.05]	0.76[0.58,1.05]	0.531
cis-beta-carotene(umol/L)	0.63[0.49,0.94]	0.65[0.52,0.91]	0.55[0.44,0.82]	<0.001	0.05[0.04,0.06]	0.04[0.04,0.07]	0.974
beta-cryptoxanthin(umol/L)	0.33[0.27,0.43]	0.34[0.27,0.44]	0.30[0.25,0.43]	0.009	0.33[0.29,0.41]	0.38[0.33,0.50]	0.002
Lutein and zeaxanthin(umol/L)	0.46[0.40,0.57]	0.50[0.45,0.59]	0.52[0.44,0.65]	<0.001	0.50[0.44,0.59]	0.51[0.42,0.65]	0.903
Creatine Phosphokinase (CPK) (IU/L)	83.00[64.00,197.00]	85.00[65.00,227.00]	78.60[58.00,188.00]	<0.001	79.00[60.00,161.00]	77.00[59.00,183.00]	0.976
Direct HDL-Cholesterol (mg/dL)	72.00[67.00,80.00]	68.00[63.00,76.00]	63.00[59.00,70.00]	<0.001	74.00[68.00,82.00]	69.00[65.00,76.00]	<0.001
Total Cholesterol(mmol/L)	6.21[5.90,6.70]	6.47[6.13,6.98]	6.28[5.90,6.90]	<0.001	6.44[6.13,6.93]	6.52[6.13,6.81]	0.753
Cholesterol, total (mmol/L)	6.21[5.90,6.70]	6.49[6.16,6.98]	6.26[5.87,6.90]	<0.001	6.44[6.10,6.85]	6.36[6.08,6.75]	0.437
Triglyceride (mg/dL)	194.00[165.00,249.00]	217.00[189.00,274.37]	264.83[228.00,357.00]	<0.001	221.46[190.00,271.00]	216.03[190.26,263.25]	0.927
Triglyceride (mmol/L)	2.19[1.86,2.81]	2.45[2.13,3.10]	2.97[2.57,3.94]	<0.001	2.51[2.15,3.06]	2.44[2.16,2.97]	0.938
LDL-cholesterol(mmol/L)	3.96[3.67,4.37]	4.19[3.93,4.68]	3.88[3.60,4.37]	<0.001	4.11[3.85,4.55]	4.22[3.90,4.53]	0.218
Glucose, serum (mmol/L)	5.61[5.44,5.94]	6.38[6.11,6.94]	7.33[5.88,9.88]	<0.001	6.99[6.49,7.88]	7.88[7.08,8.44]	<0.001
Glucose, plasma (mg/dL)	95.00[89.00,102.00]	99.00[94.00,120.00]	214.00[98.00,270.00]	<0.001	97.00[92.00,126.00]	98.00[92.00,147.77]	0.089
Plasma glucose: SI(mmol/L)	5.94[5.77,6.16]	6.72[6.49,7.07]	7.83[6.61,9.83]	<0.001	7.22[6.81,8.06]	8.16[7.48,8.71]	<0.001
C-peptide:SI(nmol/L)	1.14[1.02,1.31]	1.50[1.39,1.83]	1.81[1.62,2.06]	<0.001	1.39[1.23,1.66]	1.52[1.34,1.91]	0.003
Insulin(uU/mL)	7.37[5.16,13.99]	8.59[5.99,22.33]	9.33[6.59,31.52]	<0.001	7.93[5.70,17.82]	8.29[6.10,20.98]	0.185
Insulin:SI(pmol/L)	89.58[85.08,94.25]	77.39[53.36,126.58]	76.87[51.54,196.51]	<0.001	98.59[97.80,98.88]	70.13[44.60,116.00]	<0.001
Two Hour Glucose(OGTT)(mg/dL)	143.00[131.00,164.00]	197.00[177.00,222.00]	400.21[361.31,455.11]	<0.001	192.33[171.00,221.83]	210.57[195.80,244.74]	<0.001

Supplementary Table 5. Gender subgroup comparison of laboratory characteristics between different disease groups

Terms	Gender	Normal	Prediabetes	T2D	p	Normal	MCI	p
White blood cell count(1000 cells/uL)	female	6.90[5.70,8.40]	7.10[5.90,8.70]	7.80[6.40,9.30]	<0.001	7.00[5.90,8.10]	6.60[5.60,7.93]	0.036
	male	6.70[5.60,8.10]	7.20[6.00,8.60]	7.50[6.20,8.90]		6.90[5.70,8.44]	6.80[5.60,8.10]	
Lymphocyte percent(%)	female	29.80[24.80,35.20]	30.90[25.70,36.20]	29.70[24.02,34.80]	<0.001	28.10[22.50,34.94]	29.26[24.20,34.72]	<0.001
	male	29.80[24.80,35.00]	29.00[24.00,34.70]	27.00[22.00,32.80]		25.85[20.41,30.94]	26.10[20.90,31.42]	
Segmented neutrophils percent(%)	female	59.40[53.30,65.10]	58.00[52.10,63.80]	59.50[53.50,65.46]	<0.001	60.18[52.80,66.62]	59.20[53.20,64.50]	<0.001
	male	58.00[52.20,63.70]	58.40[51.80,64.30]	60.90[54.50,66.60]		61.74[54.60,66.80]	61.20[55.00,66.70]	
Eosinophils percent(%)	female	2.00[1.30,3.20]	2.30[1.50,3.40]	2.30[1.60,3.40]	<0.001	2.30[1.50,3.40]	2.30[1.60,3.40]	<0.001
	male	2.50[1.60,3.80]	2.70[1.80,4.00]	2.60[1.70,3.80]		2.80[1.80,4.10]	2.80[1.80,4.09]	
Basophils percent(%)	female	0.60[0.40,0.90]	0.70[0.50,0.90]	0.60[0.50,0.90]	<0.001	0.60[0.40,0.90]	0.70[0.50,0.90]	<0.001
	male	0.60[0.40,0.90]	0.70[0.40,0.90]	0.70[0.50,0.90]		0.60[0.40,0.80]	0.60[0.40,0.90]	
Lymphocyte number(1000 cells/uL)	female	2.00[1.70,2.50]	2.20[1.80,2.70]	2.20[1.80,2.80]	<0.001	1.90[1.50,2.50]	1.90[1.52,2.40]	<0.001
	male	2.00[1.60,2.40]	2.10[1.70,2.60]	2.00[1.60,2.50]		1.70[1.30,2.20]	1.70[1.40,2.10]	
Monocyte number(1000cells/uL)	female	0.50[0.40,0.60]	0.50[0.40,0.70]	0.60[0.40,0.70]	<0.001	0.50[0.40,0.70]	0.50[0.40,0.60]	<0.001
	male	0.60[0.50,0.70]	0.60[0.50,0.70]	0.60[0.50,0.70]		0.60[0.50,0.80]	0.60[0.50,0.70]	
Segmented neutrophils num(1000 cells/uL)	female	4.10[3.20,5.20]	4.10[3.20,5.30]	4.50[3.60,5.70]	<0.001	4.10[3.30,5.10]	3.90[3.10,4.80]	0.001
	male	3.90[3.00,4.90]	4.20[3.30,5.30]	4.50[3.50,5.60]		4.20[3.20,5.20]	4.00[3.30,5.00]	
Eosinophils number(1000 cells/uL)	female	0.10[0.10,0.20]	0.20[0.10,0.20]	0.20[0.10,0.30]	<0.001	0.20[0.10,0.20]	0.20[0.10,0.20]	<0.001
	male	0.20[0.10,0.30]	0.20[0.10,0.30]	0.20[0.10,0.30]		0.20[0.10,0.30]	0.20[0.10,0.30]	
Basophils number(1000 cells/uL)	female	0.00[0.00,0.10]	0.00[0.00,0.10]	0.10[0.00,0.10]	<0.001	0.00[0.00,0.10]	0.00[0.00,0.10]	0.001
	male	0.00[0.00,0.10]	0.00[0.00,0.10]	0.00[0.00,0.10]		0.00[0.00,0.10]	0.00[0.00,0.10]	
Red blood cell count(millioncells/uL)	female	4.44[4.20,4.68]	4.52[4.25,4.77]	4.51[4.22,4.82]	<0.001	4.32[4.05,4.68]	4.40[4.16,4.65]	<0.001
	male	5.01[4.75,5.26]	4.96[4.67,5.23]	4.89[4.56,5.19]		4.72[4.34,5.01]	4.74[4.46,5.01]	
Hemoglobin (g/dL)	female	13.60[12.90,14.20]	13.50[12.70,14.20]	13.40[12.50,14.20]	<0.001	13.20[12.35,14.01]	13.70[12.90,14.30]	<0.001

	male	15.40[14.70,16.00]	15.00[14.30,15.80]	14.90[13.90,15.60]		14.60[13.50,15.52]	14.80[14.10,15.60]	
Hematocrit (%)	female	39.80[37.70,41.80]	39.80[37.50,42.00]	39.30[36.90,42.00]	<0.001	39.30[36.70,42.02]	40.20[38.00,42.30]	<0.001
	male	45.20[43.20,47.20]	44.50[42.20,46.40]	43.80[41.20,46.30]		43.60[40.40,46.00]	43.80[41.40,46.00]	
Mean cell volume(fL)	female	90.20[87.00,93.10]	89.20[85.60,92.20]	88.50[84.90,91.70]	<0.001	90.50[86.90,93.86]	91.35[88.30,93.90]	<0.001
	male	90.20[87.50,93.00]	90.00[86.80,93.00]	89.60[86.50,92.70]		92.30[88.90,95.40]	92.20[89.30,94.90]	
Mean cell hemoglobin(pg)	female	30.70[29.50,31.80]	30.10[28.70,31.30]	29.90[28.40,31.10]	<0.001	30.50[29.00,31.90]	31.10[29.90,32.10]	<0.001
	male	30.80[29.80,31.90]	30.60[29.30,31.60]	30.50[29.20,31.70]		31.10[29.80,32.70]	31.40[30.40,32.60]	
Mean Cell Hgb Conc.(g/dL)	female	34.00[33.40,34.50]	33.70[33.10,34.30]	33.70[33.00,34.20]	<0.001	33.70[33.00,34.20]	34.00[33.40,34.60]	<0.001
	male	34.10[33.60,34.70]	33.80[33.30,34.40]	33.90[33.30,34.50]		33.70[33.20,34.40]	34.00[33.50,34.60]	
Red cell distribution width(%)	female	12.70 [12.20, 13.40]	13.30 [12.60, 14.00]	13.30 [12.60, 14.20]	<0.001	13.10[12.50,14.00]	12.90[12.40,13.60]	<0.001
	male	12.60 [12.20, 13.10]	13.10 [12.50, 13.70]	13.10 [12.50, 13.80]		13.30[12.70,13.99]	13.00[12.50,13.70]	
Platelet count(1000cells/uL)	female	260.00 [222.00, 304.00]	263.00 [222.00, 313.00]	261.00 [217.55, 313.97]	<0.001	244.00[202.00,295.45]	244.00[207.00,287.86]	<0.001
	male	235.00 [202.00, 272.00]	234.00 [199.00, 276.00]	223.00 [186.00, 263.00]		210.00[178.00,259.36]	218.00[182.00,253.00]	
Mean platelet volume(fL)	female	8.10 [7.60, 8.70]	8.10 [7.60, 8.80]	8.20 [7.60, 8.90]	<0.001	8.40[7.77,9.00]	8.20[7.60,8.90]	0.305
	male	8.10 [7.50, 8.60]	8.10 [7.50, 8.70]	8.20 [7.60, 8.90]		8.20[7.70,8.98]	8.20[7.60,8.90]	
Folate, RBC (nmol/L RBC)	female	850.00 [610.00, 1190.00]	1000.00 [703.00, 1409.15]	1050.00 [731.60, 1500.00]	<0.001	908.30[640.34,1279.70]	1087.20[779.00,1560.00]	<0.001
	male	806.30 [575.30, 1130.00]	900.42 [634.20, 1251.22]	1020.00 [729.28, 1450.00]		796.00[566.30,1200.44]	1010.01[740.92,1470.00]	
Folate, serum(nmol/L)	female	32.00 [22.00, 45.80]	35.30 [23.60, 55.64]	36.00 [23.95, 55.70]	<0.001	38.70[25.10,56.33]	42.60[29.46,59.80]	<0.001
	male	27.60 [19.70, 38.70]	29.50 [20.20, 43.81]	32.30 [23.10, 46.00]		29.70[19.27,40.80]	36.68[25.80,51.20]	
Vitamin B12(pmol/L)	female	343.17 [255.30, 470.11]	380.07 [276.98, 519.60]	363.10 [267.20, 528.02]	<0.001	407.46[280.99,562.14]	400.00[287.10,575.60]	<0.001
	male	350.55 [272.30, 451.70]	346.88 [262.00, 456.10]	363.10 [268.60, 492.99]		335.95[242.80,467.77]	360.90[264.90,477.90]	
Homocysteine(umol/L)	female	6.96 [5.79, 8.50]	7.94 [6.55, 9.92]	8.15 [6.25, 10.29]	<0.001	9.76[7.44,13.08]	8.62[7.13,10.61]	<0.001
	male	8.45 [7.18, 10.10]	8.97 [7.71, 11.00]	9.21 [7.56, 11.44]		11.03[9.09,13.51]	9.75[8.05,11.61]	
Blood mercury, total(nmol/L)	female	4.49 [2.30, 8.90]	4.40 [2.25, 8.48]	3.90 [2.10, 6.99]	<0.001	3.70[1.70,8.98]	5.20[2.50,10.20]	0.017
	male	4.49 [2.30, 9.20]	4.90 [2.50, 9.98]	4.00 [2.20, 9.42]		3.30[1.68,6.20]	4.90[2.80,11.59]	

Mercury, inorganic(nmol/L)	female	1.40 [1.25, 1.50]	1.25 [0.95, 1.50]	1.25 [0.95, 1.50]	<0.001	0.95[0.95,1.44]	0.95[0.95,1.70]	0.014
	male	1.25 [0.95, 1.50]	1.25 [0.95, 1.50]	1.25 [0.95, 1.50]		0.95[0.95,0.95]	0.95[0.95,1.75]	
Tot Iron Binding Capacity TIBC(umol/L)	female	63.90 [57.28, 71.96]	62.47 [56.24, 69.30]	62.48 [56.11, 69.82]	<0.001	63.09[56.19,70.61]	65.31[58.35,71.60]	<0.001
	male	60.50 [54.63, 67.30]	59.11 [53.91, 65.69]	60.00 [53.91, 66.23]		61.94[54.95,68.74]	61.93[56.03,68.80]	
Ferritin(ug/L)	female	43.00 [23.00, 78.00]	63.42 [30.81, 114.00]	75.87 [36.35, 149.30]	<0.001	97.18[53.00,154.00]	87.00[46.00,146.00]	<0.001
	male	141.00 [86.00, 227.07]	158.00 [93.00, 267.42]	162.92 [85.70, 293.81]		130.00[74.00,249.31]	134.00[70.66,232.00]	
Cotinine, Serum (ng/mL)	female	0.04 [0.01, 0.98]	0.03 [0.01, 0.50]	0.04 [0.01, 0.32]	<0.001	0.04[0.02,0.13]	0.03[0.01,0.08]	<0.001
	male	0.10 [0.02, 95.25]	0.07 [0.02, 125.00]	0.04 [0.01, 9.02]		0.09[0.02,38.27]	0.04[0.01,0.17]	
gamma-tocopherol (umol/L)	female	4.52 [2.88, 6.39]	5.09 [3.22, 7.44]	5.62 [3.70, 8.51]	<0.001	4.15[2.66,7.60]	4.32[2.35,7.06]	0.044
	male	4.71 [3.22, 6.51]	5.02 [3.39, 7.26]	5.33 [3.41, 7.70]		5.09[3.06,7.78]	4.41[2.23,7.05]	
Retinyl palmitate (umol/L)	female	0.05 [0.03, 0.08]	0.05 [0.03, 0.08]	0.05 [0.03, 0.09]	<0.001	0.05[0.04,0.09]	0.06[0.04,0.11]	<0.001
	male	0.05 [0.03, 0.09]	0.05 [0.03, 0.08]	0.06 [0.03, 0.10]		0.04[0.02,0.08]	0.07[0.04,0.11]	
Retinyl stearate (umol/L)	female	0.02 [0.01, 0.02]	0.02 [0.01, 0.02]	0.02 [0.01, 0.02]	<0.001	0.01[0.01,0.02]	0.01[0.01,0.01]	0.085
	male	0.02 [0.01, 0.02]	0.02 [0.01, 0.02]	0.02 [0.01, 0.02]		0.01[0.01,0.01]	0.01[0.01,0.02]	
Retinol (umol/L)	female	1.83 [1.51, 2.23]	1.92 [1.57, 2.31]	1.97 [1.59, 2.45]	<0.001	2.16[1.76,2.57]	2.23[1.91,2.59]	<0.001
	male	2.12 [1.80, 2.49]	2.04 [1.75, 2.43]	2.14 [1.77, 2.59]		2.08[1.76,2.63]	2.37[2.01,2.76]	
Albumin, urine(ug/mL)	female	6.60[3.30,13.20]	7.40[3.80,15.30]	10.43[4.90,28.02]	<0.001	15.22[5.46,37.33]	7.00[3.50,14.51]	<0.001
	male	6.70[3.80,11.90]	8.10[4.60,16.28]	15.70[6.70,50.00]		15.79[7.90,38.94]	8.90[4.50,20.90]	
Albumin (g/L)	female	42.00 [40.00, 44.00]	42.00 [40.00, 44.00]	41.00 [39.00, 43.00]	<0.001	42.00[40.00,44.00]	42.00[41.00,44.00]	<0.001
	male	44.00 [42.00, 46.00]	43.00 [41.00, 45.00]	42.00 [40.00, 45.00]		42.00[40.00,45.00]	43.00[41.00,45.00]	
Creatinine, urine(mg/dL)	female	93.00[49.00,150.00]	86.00[48.00,136.00]	88.00[50.00,134.00]	<0.001	81.00[46.00,123.13]	72.00[40.00,115.00]	<0.001
	male	137.00[81.00,197.00]	134.00[85.00,186.00]	118.00[80.00,169.00]		121.00[81.00,183.00]	116.00[74.00,164.00]	
Creatinine(umol/L)	female	63.65[55.69,71.60]	68.07[60.11,79.56]	67.18[56.58,80.44]	<0.001	70.72[61.00,91.05]	69.84[60.61,79.56]	<0.001
	male	83.98[76.02,94.59]	86.63[75.14,97.24]	84.86[71.60,99.01]		88.40[78.63,108.66]	88.40[79.56,100.78]	
Alanine Aminotransferase (ALT) (U/L)	female	17.00 [14.00, 22.00]	19.00 [15.00, 25.00]	20.00 [16.00, 27.00]	<0.001	18.00[15.00,22.00]	19.00[16.00,23.00]	<0.001

	male	25.00 [19.00, 33.00]	26.00 [19.00, 34.00]	25.00 [19.00, 34.00]		19.00[15.00,26.00]	22.00[18.00,28.00]	
Aspartate Aminotransferase (AST) (U/L)	female	21.00 [18.00, 24.00]	22.00 [19.00, 26.00]	22.00 [18.00, 27.00]	<0.001	22.48[20.00,27.00]	22.00[20.00,27.00]	0.001
	male	24.00 [21.00, 29.00]	25.00 [21.00, 29.00]	23.00 [20.00, 29.00]		23.00[20.00,28.00]	24.00[20.00,27.00]	
Alkaline Phosphatase (ALP) (U/L)	female	63.00 [51.00, 77.00]	71.00 [59.00, 87.00]	74.00 [59.00, 93.00]	<0.001	76.00[59.38,96.42]	69.00[57.00,83.20]	<0.001
	male	67.00 [55.00, 80.00]	68.00 [56.00, 82.00]	69.00 [56.00, 86.00]		76.00[62.00,92.00]	64.00[52.00,78.00]	
Blood urea nitrogen (mmol/L)	female	3.93 [3.21, 5.00]	4.64 [3.57, 6.07]	5.00 [3.90, 6.43]	<0.001	5.71[4.60,7.50]	5.36[4.28,6.43]	<0.001
	male	4.64 [3.93, 5.71]	5.00 [3.93, 6.07]	5.70 [4.28, 6.78]		5.40[4.60,7.14]	5.71[4.64,7.10]	
Total Calcium (mmol/L)	female	2.35 [2.28, 2.40]	2.35 [2.30, 2.40]	2.35 [2.30, 2.42]	<0.001	2.38[2.30,2.45]	2.38[2.30,2.42]	<0.001
	male	2.38 [2.33, 2.42]	2.35 [2.30, 2.40]	2.35 [2.30, 2.42]		2.35[2.30,2.40]	2.35[2.30,2.40]	
Bicarbonate (mmol/L)	female	24.00 [23.00, 26.00]	25.00 [24.00, 27.00]	25.00 [23.00, 26.00]	<0.001	25.00[23.00,26.00]	25.00[24.00,27.00]	0.051
	male	25.00[24.00,27.00]	25.00[24.00,27.00]	25.00[23.00,26.00]		25.00[23.00,27.00]	25.00[24.00,27.00]	
Gamma Glutamyl Transferase (GGT) (U/L)	female	15.00[11.00,21.00]	19.00[14.00,28.00]	23.00[16.00,36.00]	<0.001	19.51[14.00,31.00]	18.00[13.00,26.00]	<0.001
	male	22.00[16.00,33.00]	25.00[18.00,38.00]	27.00[19.00,42.00]		23.00[16.00,34.26]	22.00[16.00,30.00]	
Iron (umol/L)	female	14.10[10.40,18.60]	12.90[9.70,16.30]	12.20[9.30,15.80]	<0.001	12.72[10.11,16.66]	14.33[11.10,18.27]	<0.001
	male	16.70[13.10,21.13]	15.60[12.00,19.50]	14.87[11.60,18.60]		15.19[11.10,19.16]	15.90[12.50,19.70]	
Lactate Dehydrogenase (LDH) (U/L)	female	126.00[110.00,144.00]	138.00[121.00,158.00]	135.00[118.00,157.00]	<0.001	148.00[128.00,171.00]	138.00[123.00,155.00]	<0.001
	male	128.00[113.00,145.00]	134.00[118.00,153.00]	132.00[115.00,153.00]		138.00[120.00,160.00]	129.00[115.00,147.00]	
Phosphorus (mmol/L)	female	1.23[1.10,1.32]	1.23[1.13,1.36]	1.23[1.10,1.36]	<0.001	1.20[1.10,1.29]	1.23[1.13,1.36]	<0.001
	male	1.16[1.07,1.29]	1.16[1.03,1.29]	1.16[1.03,1.29]		1.10[0.97,1.23]	1.13[1.00,1.23]	
Bilirubin,total(umol/L)	female	10.26[6.84,11.97]	8.55[6.84,11.97]	8.55[6.84,11.97]	<0.001	10.26[8.55,11.98]	10.26[8.55,11.97]	<0.001
	male	11.97[10.26,15.39]	11.97[8.55,13.68]	11.97[8.55,13.68]		10.30[8.60,13.68]	11.97[10.26,15.39]	
Protein,total(g/L)	female	71.00[68.00,74.00]	71.00[68.00,74.00]	71.00[68.00,74.00]	<0.001	73.00[69.00,77.00]	71.00[67.00,74.00]	<0.001
	male	72.00[69.00,75.00]	72.00[69.00,75.00]	71.00[68.00,75.00]		74.00[70.00,77.00]	71.00[68.00,74.00]	
Uric acid(umol/L)	female	261.70[226.00,309.30]	303.30[255.80,350.90]	315.20[255.80,380.70]	<0.001	309.30[255.80,386.60]	303.30[255.80,356.90]	<0.001
	male	356.90[309.30,404.50]	362.80[315.20,416.40]	345.00[285.50,410.40]		356.90[303.30,416.40]	356.90[303.30,410.40]	

Sodium(mmol/L)	female	139.00[138.00,140.00]	139.00[138.00,141.00]	139.00[137.00,141.00]	<0.001	139.91[138.00,141.00]	140.00[138.00,141.00]	0.889
	male	140.00[138.00,141.00]	139.00[138.00,141.00]	139.00[137.00,140.67]		140.00[138.00,141.00]	140.00[138.00,141.00]	
Potassium(mmol/L)	female	3.90[3.70,4.10]	4.00[3.80,4.20]	4.00[3.80,4.29]	<0.001	4.10[3.80,4.31]	4.00[3.80,4.28]	<0.001
	male	4.00[3.80,4.20]	4.10[3.90,4.30]	4.10[3.90,4.38]		4.20[3.95,4.50]	4.14[3.90,4.40]	
Chloride(mmol/L)	female	104.00[102.00,106.00]	103.00[101.00,105.00]	102.00[100.00,105.00]	<0.001	103.00[100.00,105.00]	103.00[101.00,105.00]	0.002
	male	103.00[101.00,105.00]	103.00[101.00,105.00]	102.00[100.00,104.00]		103.00[100.80,105.00]	103.90[102.00,105.00]	
Transferrin Saturation (%)	female	22.60[15.90,30.10]	21.00[15.30,27.00]	21.00[15.20,27.00]	<0.001	21.00[15.17,27.16]	22.05[17.32,28.93]	<0.001
	male	28.00[21.80,36.00]	26.50[21.00,34.00]	25.00[19.50,31.70]		24.39[17.20,32.47]	26.02[20.30,32.80]	
Globulin (g/L)	female	29.00[26.00,32.00]	29.00[27.00,33.00]	30.61[28.00,34.00]	<0.001	31.00[27.00,35.00]	28.00[25.00,31.00]	<0.001
	male	28.00[25.00,30.00]	29.00[26.00,32.00]	29.00[26.00,32.00]		31.00[28.00,34.00]	27.00[25.00,31.00]	
alpha-carotene(umol/L)	female	0.06[0.03,0.12]	0.05[0.03,0.10]	0.05[0.03,0.09]	<0.001	0.05[0.04,0.11]	0.07[0.04,0.12]	0.003
	male	0.04[0.02,0.09]	0.04[0.03,0.09]	0.04[0.02,0.07]		0.04[0.02,0.07]	0.06[0.03,0.10]	
trans-beta-carotene(umol/L)	female	0.27[0.15,0.49]	0.26[0.16,0.44]	0.21[0.11,0.38]	<0.001	0.37[0.21,0.59]	0.37[0.22,0.59]	0.001
	male	0.19[0.12,0.35]	0.20[0.12,0.35]	0.16[0.09,0.32]		0.20[0.09,0.34]	0.31[0.18,0.50]	
cis-beta-carotene(umol/L)	female	0.02[0.01,0.03]	0.02[0.01,0.03]	0.01[0.01,0.02]	<0.001	0.02[0.01,0.04]	0.02[0.01,0.04]	<0.001
	male	0.01[0.01,0.02]	0.01[0.01,0.02]	0.01[0.01,0.02]		0.01[0.01,0.02]	0.02[0.01,0.03]	
beta-cryptoxanthin(umol/L)	female	0.13[0.08,0.21]	0.12[0.07,0.20]	0.11[0.06,0.18]	<0.001	0.16[0.09,0.29]	0.16[0.10,0.26]	<0.001
	male	0.13[0.08,0.20]	0.12[0.07,0.20]	0.10[0.06,0.17]		0.10[0.05,0.18]	0.14[0.08,0.21]	
Lutein and zeaxanthin(umol/L)	female	0.26[0.18,0.36]	0.26[0.19,0.38]	0.25[0.18,0.38]	0.011	0.30[0.20,0.41]	0.28[0.20,0.40]	0.002
	male	0.25[0.18,0.35]	0.28[0.20,0.38]	0.26[0.18,0.35]		0.21[0.16,0.32]	0.27[0.19,0.37]	
trans-lycopene(umol/L)	female	0.40[0.28,0.53]	0.36[0.25,0.50]	0.34[0.22,0.47]	<0.001	0.32[0.23,0.40]	0.35[0.22,0.50]	0.127
	male	0.43[0.31,0.58]	0.39[0.26,0.57]	0.35[0.22,0.50]		0.27[0.15,0.45]	0.33[0.21,0.48]	
VitaminD(nmol/L)	female	61.60[46.80,77.80]	54.40[39.80,68.90]	51.90[37.50,68.00]	<0.001	51.60[39.70,70.60]	58.70[46.80,75.40]	0.063
	male	63.10[50.80,76.20]	56.06[43.40,68.20]	55.70[42.00,68.90]		58.70[44.40,70.60]	63.50[51.60,73.00]	
Creatine Phosphokinase (CPK) (IU/L)	female	82.00[61.00,114.00]	92.00[66.00,131.00]	79.00[54.00,119.00]	<0.001	91.04[59.86,136.04]	82.00[59.26,111.00]	<0.001

	male	140.00[98.00,215.00]	150.00[101.00,230.00]	117.00[83.00,191.00]		106.59[69.92,169.18]	117.00[82.00,174.00]	
Direct HDL-Cholesterol(mmol/L)	female	1.53[1.27,1.81]	1.40[1.16,1.71]	1.27[1.06,1.50]	<0.001	1.42[1.19,1.73]	1.50[1.27,1.84]	<0.001
	male	1.22[1.03,1.45]	1.16[0.98,1.37]	1.09[0.91,1.27]		1.16[1.01,1.37]	1.24[1.03,1.50]	
Direct HDL-Cholesterol (mg/dL)	female	58.00[48.00,69.00]	53.00[45.00,65.00]	48.00[41.00,58.00]	<0.001	55.00[45.00,67.00]	57.00[48.00,70.00]	<0.001
	male	46.00[39.00,56.00]	44.00[37.00,53.00]	41.00[35.00,48.00]		44.00[38.00,53.00]	46.00[39.00,56.00]	
Total Cholesterol(mmol/L)	female	4.99[4.34,5.69]	5.30[4.65,6.00]	4.94[4.22,5.74]	<0.001	5.38[4.60,6.21]	5.43[4.81,6.15]	<0.001
	male	4.91[4.24,5.61]	5.07[4.37,5.79]	4.55[3.85,5.40]		4.81[4.11,5.60]	4.84[4.14,5.52]	
Cholesterol, total (mmol/L)	female	4.99 [4.34, 5.72]	5.30 [4.65, 6.03]	4.91 [4.19, 5.72]	<0.001	5.28[4.55,6.13]	5.40[4.75,6.10]	<0.001
	male	4.91 [4.27, 5.61]	5.04 [4.37, 5.82]	4.53 [3.83, 5.40]		4.73[4.02,5.51]	4.81[4.06,5.48]	
Triglyceride (mg/dL)	female	90.00 [63.00, 130.00]	115.00 [82.00, 165.00]	142.00 [99.00, 200.00]	<0.001	121.64[82.41,171.71]	123.16[86.00,172.00]	0.445
	male	105.00 [73.00, 156.00]	118.00 [84.00, 174.00]	141.00 [94.00, 208.00]		112.11[81.00,153.15]	114.33[79.00,168.49]	
Triglyceride (mmol/L)	female	1.02 [0.71, 1.47]	1.30 [0.93, 1.86]	1.60 [1.12, 2.26]	<0.001	1.37[0.93,1.94]	1.39[0.97,1.94]	0.445
	male	1.19 [0.82, 1.76]	1.33 [0.95, 1.96]	1.59 [1.06, 2.35]		1.26[0.91,1.73]	1.30[0.89,1.90]	
LDL-cholesterol(mmol/L)	female	2.85 [2.30, 3.49]	3.08 [2.53, 3.72]	2.71 [2.07, 3.41]	<0.001	2.93[2.33,3.62]	3.10[2.56,3.75]	<0.001
	male	2.95 [2.38, 3.54]	3.08 [2.46, 3.70]	2.48 [1.94, 3.18]		2.79[2.20,3.57]	2.87[2.20,3.43]	
Glycohemoglobin(%)	female	5.20[5.00,5.40]	5.80[5.70,6.00]	6.90[6.30,7.90]	<0.001	152.55(57.67)	133.92(51.11)	0.001
	male	5.30[5.10,5.40]	5.80[5.70,6.00]	7.10[6.50,8.20]		167.38(78.03)	126.71(50.60)	
Glucose, serum (mmol/L)	female	4.83[4.50,5.16]	5.33[4.94,5.83]	7.05[5.77,9.60]	<0.001	5.50[5.05,6.37]	5.27[4.88,5.83]	<0.001
	male	5.00[4.66,5.38]	5.44[5.00,5.94]	7.66[6.00,10.44]		5.61[5.11,6.66]	5.44[5.00,6.16]	
Glucose, plasma (mg/dL)	female	93.00 [88.00, 99.00]	104.00 [97.00, 111.60]	134.00 [115.00, 172.00]	<0.001	106.00[95.89,123.21]	102.00[94.40,111.09]	<0.001
	male	98.00 [92.00, 104.00]	107.00 [99.86, 115.00]	149.00 [124.95, 193.94]		107.00[96.38,129.00]	105.00[97.20,116.16]	
Plasma glucose: SI(mmol/L)	female	5.16 [4.88, 5.50]	5.77 [5.38, 6.19]	7.44 [6.38, 9.55]	<0.001	5.88[5.33,6.84]	5.66[5.24,6.17]	<0.001
	male	5.44 [5.11, 5.77]	5.94 [5.54, 6.38]	8.27 [6.94, 10.75]		5.94[5.35,7.16]	5.83[5.40,6.45]	
C-peptide:SI(nmol/L)	female	0.65 [0.49, 0.87]	0.94 [0.73, 1.30]	1.02 [0.76, 1.28]	<0.001	0.99[0.64,1.35]	0.81[0.60,1.05]	0.016
	male	0.67 [0.51, 0.93]	1.00 [0.76, 1.31]	1.12 [0.79, 1.57]		0.90[0.62,1.18]	0.82[0.64,1.16]	

Insulin(uU/mL)	female	7.99 [5.33, 12.11]	11.61 [7.53, 18.30]	14.24 [9.21, 23.23]	<0.001	11.52[7.01,16.59]	9.90[6.38,14.78]	0.061
	male	8.60 [5.66, 13.59]	11.96 [7.06, 18.95]	13.84 [8.18, 23.72]		11.21[6.81,16.05]	10.05[6.71,15.67]	
Insulin:SI(pmol/L)	female	51.18 [38.04, 73.11]	82.91 [56.32, 122.50]	110.68 [65.48, 145.67]	<0.001	71.99[47.06,130.42]	59.85[41.40,84.80]	0.055
	male	54.47 [39.72, 78.82]	83.74 [53.26, 115.69]	107.82 [61.68, 184.27]		67.21[43.53,91.96]	60.16[43.93,94.06]	
Two Hour Glucose(OGTT)(mg/dL)	female	100.00[83.00,121.00]	128.00[104.00,163.00]	265.77[186.67,320.00]	<0.001	139.00[107.96,185.76]	123.00[99.53,157.87]	0.001
	male	99.00[81.00,121.00]	122.00[95.00,156.00]	274.66[218.12,334.35]		150.00[112.74,196.58]	117.00[91.76,154.00]	

Supplementary Table 6. Age subgroup comparison of laboratory characteristics between different disease groups

Terms	Age	Normal	Prediabetes	T2D	p
White blood cell count(1000 cells/uL)	old	6.50[5.50,7.70]	6.90[5.90,8.20]	7.40[6.10,8.80]	<0.001
	young	6.90[5.70,8.40]	7.40[6.10,9.00]	7.80[6.40,9.30]	
Lymphocyte percent(%)	old	27.80[22.60,33.20]	28.60[23.10,34.40]	27.00[21.80,33.00]	<0.001
	young	30.20[25.20,35.40]	31.10[26.10,36.40]	29.42[24.00,35.10]	
Segmented neutrophils percent(%)	old	59.90[53.80,65.40]	58.90[52.50,64.90]	60.70[54.40,66.30]	<0.001
	young	58.60[52.50,64.20]	57.70[51.60,63.40]	59.75[53.40,65.70]	
Eosinophils percent(%)	old	2.50[1.70,3.70]	2.60[1.70,3.90]	2.60[1.80,3.80]	<0.001
	young	2.20[1.40,3.40]	2.30[1.60,3.60]	2.30[1.60,3.40]	
Basophils percent(%)	old	0.70[0.50,0.90]	0.70[0.50,0.90]	0.70[0.50,0.90]	<0.001
	young	0.60[0.40,0.90]	0.70[0.40,0.90]	0.60[0.40,0.90]	
Lymphocyte number(1000 cells/uL)	old	1.80[1.40,2.20]	1.90[1.60,2.40]	2.00[1.50,2.50]	<0.001
	young	2.00[1.70,2.50]	2.30[1.80,2.80]	2.20[1.80,2.80]	
Monocyte number(1000cells/uL)	old	0.50[0.40,0.70]	0.60[0.50,0.70]	0.60[0.50,0.70]	<0.001
	young	0.50[0.40,0.60]	0.60[0.40,0.70]	0.60[0.40,0.70]	
Segmented neutrophils num(1000 cells/uL)	old	3.80[3.10,4.80]	4.00[3.20,5.00]	4.40[3.50,5.50]	<0.001
	young	4.00[3.10,5.10]	4.20[3.20,5.50]	4.60[3.60,5.70]	
Eosinophils number(1000 cells/uL)	old	0.20[0.10,0.20]	0.20[0.10,0.30]	0.20[0.10,0.30]	<0.001
	young	0.20[0.10,0.20]	0.20[0.10,0.30]	0.20[0.10,0.30]	
Basophils number(1000 cells/uL)	old	0.00[0.00,0.10]	0.00[0.00,0.10]	0.10[0.00,0.10]	<0.001
	young	0.00[0.00,0.10]	0.00[0.00,0.10]	0.10[0.00,0.10]	
Red blood cell count(millioncells/uL)	old	4.57[4.26,4.87]	4.60[4.30,4.91]	4.59[4.24,4.91]	<0.001
	young	4.72[4.40,5.07]	4.80[4.49,5.13]	4.82[4.49,5.14]	
Hemoglobin (g/dL)	old	14.20[13.40,15.10]	14.10[13.20,15.00]	13.90[12.90,14.90]	<0.001

	young	14.50[13.50,15.50]	14.30[13.30,15.30]	14.40[13.30,15.40]	
Hematocrit (%)	old	41.80[39.20,44.60]	41.60[38.80,44.30]	40.90[37.70,43.90]	<0.001
	young	42.50[39.30,45.50]	42.40[39.20,45.30]	42.40[39.20,45.20]	
Mean cell volume(fL)	old	92.20[89.30,95.07]	91.00[88.10,93.70]	90.10[86.90,93.10]	<0.001
	young	89.80[86.90,92.60]	88.40[84.90,91.40]	88.01[84.70,91.10]	
Mean cell hemoglobin(pg)	old	31.30[30.20,32.40]	30.80[29.70,31.90]	30.40[29.10,31.70]	<0.001
	young	30.70[29.50,31.70]	30.00[28.50,31.20]	30.00[28.60,31.10]	
Mean Cell Hgb Conc.(g/dL)	old	33.90[33.40,34.50]	33.80[33.20,34.30]	33.80[33.10,34.30]	<0.001
	young	34.00[33.50,34.60]	33.80[33.20,34.40]	33.90[33.30,34.50]	
Red cell distribution width(%)	old	12.90[12.40,13.60]	13.30[12.70,13.90]	13.40[12.70,14.10]	<0.001
	young	12.60[12.10,13.20]	13.10[12.50,13.90]	13.10[12.40,13.80]	
Platelet count(1000cells/uL)	old	233.00[196.00,273.00]	236.00[199.00,279.00]	228.00[190.00,274.00]	<0.001
	young	249.00[214.00,292.00]	259.00[219.00,306.00]	255.00[212.00,306.00]	
Mean platelet volume(fL)	old	8.10[7.50,8.70]	8.10[7.50,8.70]	8.20[7.60,8.90]	<0.001
	young	8.10[7.60,8.70]	8.10[7.60,8.80]	8.20[7.60,8.90]	
Folate, RBC (nmol/L RBC)	old	1014.70[733.90,1490.00]	1080.00[752.97,1550.00]	1090.00[770.06,1570.00]	<0.001
	young	801.80[573.00,1118.25]	887.18[627.00,1200.00]	971.02[697.87,1370.00]	
Folate, serum(nmol/L)	old	41.60[27.40,60.70]	41.40[27.40,63.20]	38.20[26.30,60.70]	<0.001
	young	28.50[20.00,39.90]	27.60[19.60,40.70]	30.40[21.60,42.60]	
Vitamin B12(pmol/L)	old	374.90[270.85,519.55]	370.37[264.94,514.85]	360.27[260.60,521.25]	<0.001
	young	343.17[262.73,451.70]	357.91[270.81,470.10]	363.82[275.30,497.41]	
Homocysteine(umol/L)	old	9.38[7.76,11.61]	9.58[8.03,11.62]	9.82[7.84,12.25]	<0.001
	young	7.44[6.22,8.94]	7.86[6.58,9.39]	7.89[6.18,9.42]	
Blood mercury, total(nmol/L)	old	5.49[2.70,10.98]	5.00[2.50,9.30]	3.99[2.25,8.48]	<0.001
	young	4.30[2.20,8.52]	4.31[2.20,8.98]	3.99[2.00,7.90]	

Mercury, inorganic(nmol/L)	old	1.25[1.25,1.60]	1.25[0.95,1.50]	1.25[0.95,1.50]	<0.001
	young	1.25[1.25,1.50]	1.25[0.95,1.50]	1.25[0.95,1.50]	
Tot Iron Binding Capacity TIBC(umol/L)	old	59.44[53.73,67.30]	59.64[54.09,65.87]	60.14[53.55,66.23]	<0.001
	young	63.01[56.60,70.53]	61.93[56.06,68.38]	62.47[56.39,70.48]	
Ferritin(ug/L)	old	108.00[56.00,185.00]	109.36[64.00,188.66]	123.00[62.00,230.93]	<0.001
	young	61.00[28.60,122.00]	79.90[34.00,158.00]	99.80[42.31,206.00]	
Cotinine, Serum (ng/mL)	old	0.03[0.01,0.12]	0.03[0.01,0.20]	0.03[0.01,0.17]	<0.001
	young	0.07[0.02,48.60]	0.08[0.02,120.25]	0.06[0.02,27.41]	
gamma-tocopherol (umol/L)	old	3.77[2.20,6.10]	4.32[2.69,6.56]	4.68[2.98,7.16]	<0.001
	young	4.73[3.24,6.51]	5.55[3.96,7.81]	6.17[4.13,9.10]	
Retinyl palmitate (umol/L)	old	0.06[0.03,0.09]	0.05[0.03,0.09]	0.06[0.03,0.10]	<0.001
	young	0.05[0.03,0.09]	0.05[0.03,0.08]	0.05[0.03,0.09]	
Retinyl stearate (umol/L)	old	0.02[0.01,0.02]	0.02[0.01,0.02]	0.02[0.01,0.02]	<0.001
	young	0.02[0.01,0.02]	0.02[0.01,0.02]	0.02[0.01,0.02]	
Retinol (umol/L)	old	2.19[1.84,2.59]	2.10[1.77,2.51]	2.22[1.80,2.65]	<0.001
	young	1.94[1.60,2.33]	1.90[1.58,2.27]	1.92[1.58,2.34]	
Albumin, urine(ug/mL)	old	7.30[3.70,14.90]	8.20[4.20,17.30]	14.00[6.10,42.50]	<0.001
	young	6.60[3.40,12.20]	7.50[4.10,15.00]	11.80[5.40,31.38]	
Albumin (g/L)	old	42.00[41.00,44.00]	42.00[40.00,44.00]	42.00[39.00,44.00]	<0.001
	young	44.00[41.00,46.00]	42.00[40.00,44.00]	42.00[39.00,44.00]	
Creatinine, urine(mg/dL)	old	88.14[50.00,137.00]	95.00[53.00,143.00]	99.00[61.00,146.00]	<0.001
	young	119.00[64.00,180.00]	120.00[68.00,179.00]	107.00[67.00,162.00]	
Creatinine(umol/L)	old	79.56[66.30,92.82]	79.56[68.07,95.47]	83.10[70.70,103.43]	<0.001
	young	71.60[61.88,85.75]	73.37[61.90,86.63]	70.72[59.23,84.86]	
Alanine Aminotransferase (ALT) (U/L)	old	19.00[16.00,25.00]	20.00[16.00,25.00]	21.00[16.00,27.00]	<0.001

	young	21.00[16.00,29.00]	24.00[18.00,33.00]	25.00[19.00,36.00]	
Aspartate Aminotransferase (AST) (U/L)	old	23.00[20.00,27.00]	23.00[20.00,27.00]	22.00[19.00,27.00]	<0.001
	young	22.00[19.00,27.00]	23.00[19.00,28.00]	23.00[19.00,29.00]	
Alkaline Phosphatase (ALP) (U/L)	old	68.00[57.00,83.00]	70.00[57.00,85.00]	70.00[56.00,87.00]	<0.001
	young	64.00[52.00,78.00]	69.75[58.00,84.00]	73.00[58.00,91.00]	
Blood urea nitrogen (mmol/L)	old	5.36[4.28,6.78]	5.71[4.64,6.78]	6.07[4.64,7.50]	<0.001
	young	4.28[3.21,5.36]	4.30[3.57,5.36]	4.64[3.57,5.71]	
Total Calcium (mmol/L)	old	2.35[2.30,2.42]	2.35[2.30,2.42]	2.38[2.30,2.42]	<0.001
	young	2.35[2.30,2.42]	2.35[2.30,2.40]	2.35[2.30,2.42]	
Bicarbonate (mmol/L)	old	25.00[24.00,27.00]	26.00[24.00,27.00]	25.00[23.00,27.00]	<0.001
	young	25.00[23.00,26.00]	25.00[23.00,26.00]	25.00[23.00,26.00]	
Gamma Glutamyl Transferase (GGT) (U/L)	old	19.00[14.00,27.00]	20.00[15.00,28.00]	22.00[16.00,34.00]	<0.001
	young	18.00[13.00,28.00]	24.00[17.00,36.00]	28.00[19.00,44.00]	
Iron (umol/L)	old	15.58[12.18,19.20]	14.50[11.30,18.10]	13.40[10.57,17.00]	<0.001
	young	15.40[11.60,20.10]	13.80[10.20,18.10]	13.60[10.40,17.62]	
Lactate Dehydrogenase (LDH) (U/L)	old	138.00[123.00,157.00]	140.00[123.00,160.00]	136.00[118.00,158.00]	<0.001
	young	125.00[110.00,142.00]	133.00[117.24,153.00]	131.00[115.00,151.00]	
Phosphorus (mmol/L)	old	1.19[1.07,1.29]	1.20[1.10,1.32]	1.19[1.07,1.32]	<0.001
	young	1.20[1.10,1.32]	1.20[1.07,1.32]	1.20[1.07,1.32]	
Bilirubin,total(umol/L)	old	11.97[8.55,13.70]	10.26[8.55,13.68]	10.26[8.55,13.68]	<0.001
	young	10.30[8.55,13.68]	10.26[6.84,11.97]	10.26[6.84,13.68]	
Protein,total(g/L)	old	11.97[8.55,13.70]	10.26[8.55,13.68]	10.26[8.55,13.68]	<0.001
	young	10.30[8.55,13.68]	10.26[6.84,11.97]	10.26[6.84,13.68]	
Uric acid(umol/L)	old	321.20[267.70,374.70]	333.10[279.60,392.60]	345.00[285.50,410.40]	<0.001
	young	309.30[249.80,368.80]	333.10[279.60,386.60]	315.20[261.70,380.70]	

Sodium(mmol/L)	old	140.00[138.00,141.00]	140.00[138.00,141.00]	139.00[138.00,141.00]	<0.001
	young	139.00[138.00,141.00]	139.00[138.00,141.00]	138.00[137.00,140.00]	
Potassium(mmol/L)	old	4.10[3.81,4.30]	4.10[3.80,4.30]	4.10[3.90,4.40]	<0.001
	young	4.00[3.80,4.20]	4.00[3.80,4.20]	4.00[3.80,4.20]	
Chloride(mmol/L)	old	103.00[101.00,105.00]	103.00[101.00,105.00]	102.00[100.00,105.00]	<0.001
	young	104.00[102.00,105.00]	104.00[102.00,105.00]	102.00[100.00,104.00]	
Transferrin Saturation (%)	old	26.10[20.10,33.00]	25.00[19.50,31.00]	24.00[17.80,29.00]	<0.001
	young	24.20[17.70,32.70]	22.80[16.29,29.00]	22.02[16.26,29.00]	
Globulin (g/L)	old	28.00[25.00,31.00]	29.00[26.00,32.00]	29.00[26.00,32.00]	<0.001
	young	28.00[26.00,31.00]	29.00[27.00,32.01]	30.00[27.00,33.00]	
alpha-carotene(umol/L)	old	0.07[0.04,0.12]	0.06[0.03,0.11]	0.05[0.02,0.08]	<0.001
	young	0.05[0.03,0.10]	0.04[0.02,0.09]	0.04[0.02,0.07]	
trans-beta-carotene(umol/L)	old	0.34[0.19,0.57]	0.29[0.17,0.51]	0.22[0.12,0.40]	<0.001
	young	0.21[0.13,0.38]	0.19[0.11,0.34]	0.15[0.08,0.26]	
cis-beta-carotene(umol/L)	old	0.02[0.01,0.04]	0.02[0.01,0.03]	0.01[0.01,0.02]	<0.001
	young	0.01[0.01,0.02]	0.01[0.01,0.02]	0.01[0.01,0.02]	
beta-cryptoxanthin(umol/L)	old	0.14[0.08,0.22]	0.12[0.07,0.20]	0.10[0.06,0.16]	<0.001
	young	0.13[0.09,0.20]	0.12[0.07,0.20]	0.10[0.07,0.18]	
Lutein and zeaxanthin(umol/L)	old	0.29[0.20,0.41]	0.29[0.21,0.41]	0.26[0.18,0.37]	<0.001
	young	0.25[0.18,0.35]	0.25[0.18,0.35]	0.25[0.18,0.36]	
trans-lycopene(umol/L)	old	0.34[0.22,0.48]	0.33[0.22,0.48]	0.30[0.19,0.43]	<0.001
	young	0.43[0.31,0.56]	0.42[0.29,0.58]	0.38[0.28,0.53]	
VitaminD(nmol/L)	old	63.50[49.50,75.40]	58.81[46.80,73.00]	55.70[42.20,68.90]	<0.001
	young	62.47[48.30,77.70]	51.90[38.50,65.80]	51.90[39.70,66.50]	
Creatine Phosphokinase (CPK) (IU/L)	old	95.00[65.00,133.00]	100.00[71.00,155.34]	95.00[65.00,144.12]	<0.001

	young	107.00[75.00,166.00]	125.00[84.00,200.00]	106.00[70.00,172.60]	
Direct HDL-Cholesterol(mmol/L)	old	1.47[1.21,1.84]	1.37[1.14,1.68]	1.19[1.01,1.45]	<0.001
	young	1.34[1.11,1.63]	1.22[1.01,1.47]	1.14[0.96,1.34]	
Direct HDL-Cholesterol (mg/dL)	old	56.00[46.00,70.00]	52.00[43.00,64.00]	46.00[38.00,56.00]	<0.001
	young	51.00[42.00,62.00]	47.00[39.00,56.00]	43.00[37.00,52.00]	
Total Cholesterol(mmol/L)	old	5.25[4.60,5.95]	5.12[4.45,5.84]	4.50[3.85,5.33]	<0.001
	young	4.89[4.24,5.61]	5.25[4.58,5.95]	5.02[4.24,5.82]	
Cholesterol, total (mmol/L)	old	5.25[4.58,5.97]	5.12[4.42,5.87]	4.47[3.83,5.30]	<0.001
	young	4.89[4.27,5.61]	5.25[4.58,5.92]	4.99[4.24,5.79]	
Triglyceride (mg/dL)	old	105.00[75.00,149.00]	116.00[84.00,166.00]	134.00[94.43,192.47]	<0.001
	young	105.00[75.00,149.00]	116.00[84.00,166.00]	134.00[94.43,192.47]	
Triglyceride (mmol/L)	old	1.19[0.85,1.68]	1.31[0.95,1.87]	1.51[1.07,2.18]	<0.001
	young	1.07[0.74,1.59]	1.32[0.91,1.94]	1.69[1.12,2.45]	
LDL-cholesterol(mmol/L)	old	3.05[2.48,3.65]	2.92[2.34,3.57]	2.33[1.84,3.08]	<0.001
	young	2.87[2.33,3.47]	3.18[2.61,3.83]	2.82[2.25,3.52]	
Glycohemoglobin(%)	old	5.40[5.20,5.50]	5.90[5.70,6.00]	6.80[6.40,7.60]	<0.001
	young	5.20[5.00,5.40]	5.80[5.70,6.00]	7.10[6.50,8.70]	
Glucose, serum (mmol/L)	old	5.11[4.83,5.50]	5.44[5.05,6.00]	7.11[5.88,9.33]	<0.001
	young	4.88[4.55,5.22]	5.33[4.88,5.77]	7.77[5.88,11.30]	
Glucose, plasma (mg/dL)	old	99.00[93.00,106.10]	107.00[100.00,116.00]	137.94[120.00,169.00]	<0.001
	young	95.00[89.00,101.00]	104.00[97.00,111.40]	149.49[119.00,206.03]	
Plasma glucose: SI(mmol/L)	old	5.50[5.16,5.89]	5.94[5.55,6.44]	7.66[6.66,9.38]	<0.001
	young	5.27[4.94,5.61]	5.77[5.38,6.18]	8.30[6.61,11.44]	
C-peptide:SI(nmol/L)	old	0.74[0.57,1.00]	1.00[0.76,1.34]	1.07[0.81,1.36]	<0.001
	young	0.65[0.49,0.87]	0.95[0.73,1.27]	1.05[0.76,1.46]	

Insulin(uU/mL)	old	8.08[5.40,12.28]	10.69[6.59,17.30]	12.79[8.27,21.55]	<0.001
	young	8.26[5.49,12.85]	13.01[7.83,19.65]	15.40[9.06,25.55]	
Insulin:SI(pmol/L)	old	52.86[39.96,72.80]	77.63[51.89,112.91]	103.42[63.90,156.68]	<0.001
	young	53.34[38.45,75.38]	86.22[56.59,120.00]	115.86[63.82,159.45]	
Two Hour Glucose(OGTT)(mg/dL)	old	115.00[94.00,141.00]	137.00[110.00,175.92]	261.75[200.00,308.00]	<0.001
	young	97.00[81.00,117.00]	118.00[95.00,146.00]	272.88[197.49,352.00]	

Old: age ≥60，young: age＜60.

Supplementary Table 7. Ethnicity subgroup comparison of laboratory characteristics between different disease groups

Terms	Ethnicity	Normal	Prediabetes	T2D	p	Normal	MCI	p
White blood cell count(1000 cells/uL)	Mexican American	7.20[6.10,8.60]	7.40[6.30,8.90]	7.60[6.50,8.90]	<0.001	7.14[6.10,8.80]	7.03[5.80,8.10]	<0.001
	Other Hispanic	7.10[6.00,8.40]	7.40[6.20,8.70]	7.70[6.40,9.00]		6.88[5.80,7.93]	6.98[5.70,8.20]	
	Non-Hispanic White	6.90[5.70,8.30]	7.40[6.10,8.80]	7.80[6.40,9.30]		7.10[6.10,8.23]	6.70[5.70,8.00]	
	Non-Hispanic Black	6.10[4.90,7.60]	6.40[5.10,7.90]	6.80[5.60,8.40]		6.10[4.90,7.30]	6.10[4.90,7.40]	
	Other Race - Including Multi-Racial	6.80[5.60,8.20]	6.90[5.90,8.60]	7.50[6.10,8.90]		6.90[5.83,7.88]	6.60[5.60,8.00]	
Lymphocyte percent(%)	Mexican American	30.40[25.50,35.40]	30.52[26.40,35.80]	29.80[24.60,35.10]	<0.001	29.10[22.70,34.60]	29.40[25.00,33.61]	<0.001
	Other Hispanic	29.90[25.40,35.17]	31.30[26.15,35.99]	29.20[23.80,35.13]		30.77[24.84,36.22]	29.80[24.41,35.51]	
	Non-Hispanic White	29.20[24.30,34.20]	28.70[23.60,33.70]	26.70[21.80,32.10]		24.80[20.00,29.64]	27.30[22.50,32.70]	
	Non-Hispanic Black	34.50[27.90,41.30]	34.72[28.60,41.70]	32.60[26.50,39.70]		31.30[25.20,38.45]	33.80[27.43,40.20]	
	Other Race - Including Multi-Racial	30.70[25.50,36.66]	32.30[26.50,37.20]	29.80[24.71,35.20]		28.83[23.09,35.13]	30.49[23.96,35.40]	
Segmented neutrophils percent(%)	Mexican American	58.80[53.30,64.60]	58.40[52.70,63.30]	59.69[53.70,65.10]	<0.001	59.78[53.70,66.20]	59.63[53.80,64.40]	<0.001
	Other Hispanic	58.40[52.80,64.20]	56.85[51.75,63.00]	59.10[53.17,65.58]		56.62[52.10,62.70]	59.06[52.32,64.10]	
	Non-Hispanic White	59.30[53.40,64.70]	59.50[53.60,65.00]	61.60[55.60,67.00]		63.20[57.60,68.00]	60.50[54.30,65.86]	
	Non-Hispanic Black	53.50[46.00,61.30]	53.00[45.60,60.30]	56.00[48.70,62.70]		55.20[48.07,62.80]	53.90[47.00,61.30]	
	Other Race - Including Multi-Racial	57.80[51.80,63.90]	56.44[50.90,61.70]	58.99[52.73,64.40]		60.00[51.10,63.84]	57.00[51.81,65.60]	
Eosinophils percent(%)	Mexican American	2.00[1.30,3.20]	2.30[1.60,3.40]	2.40[1.50,3.30]	<0.001	2.50[1.70,3.50]	2.50[1.60,3.50]	0.085
	Other Hispanic	2.20[1.40,3.50]	2.30[1.60,3.80]	2.50[1.70,3.80]		2.80[1.90,4.16]	2.30[1.60,3.70]	
	Non-Hispanic White	2.30[1.50,3.40]	2.50[1.70,3.70]	2.50[1.70,3.70]		2.50[1.60,3.50]	2.50[1.70,3.80]	
	Non-Hispanic Black	2.20[1.30,3.40]	2.30[1.50,3.60]	2.20[1.40,3.30]		2.60[1.50,3.78]	2.30[1.60,3.70]	
	Other Race - Including Multi-Racial	2.30[1.50,3.70]	2.60[1.70,4.10]	2.50[1.70,3.70]		2.64[1.47,5.02]	2.40[1.60,3.59]	
Basophils percent(%)	Mexican American	0.60[0.40,0.80]	0.60[0.40,0.90]	0.60[0.40,0.90]	<0.001	0.60[0.40,0.90]	0.60[0.45,0.90]	<0.001
	Other Hispanic	0.60[0.40,0.80]	0.70[0.50,0.90]	0.60[0.42,0.90]		0.60[0.40,0.90]	0.60[0.40,0.80]	
	Non-Hispanic White	0.60[0.40,0.90]	0.70[0.50,0.90]	0.70[0.50,0.90]		0.60[0.40,0.80]	0.70[0.40,0.90]	

	Non-Hispanic Black	0.60[0.40,0.90]	0.70[0.40,0.90]	0.60[0.40,0.90]		0.60[0.40,0.90]	0.60[0.40,0.90]	
	Other Race - Including Multi-Racial	0.60[0.40,0.90]	0.70[0.50,0.90]	0.70[0.50,0.90]		0.60[0.40,0.88]	0.70[0.40,0.90]	
Lymphocyte number(1000 cells/uL)	Mexican American	2.10[1.80,2.60]	2.30[1.90,2.70]	2.20[1.80,2.70]	<0.001	2.00[1.60,2.50]	2.00[1.70,2.40]	<0.001
	Other Hispanic	2.10[1.80,2.50]	2.30[1.80,2.70]	2.20[1.80,2.80]		2.06[1.70,2.50]	2.06[1.60,2.40]	
	Non-Hispanic White	2.00[1.60,2.40]	2.10[1.70,2.50]	2.00[1.60,2.60]		1.70[1.30,2.20]	1.80[1.40,2.20]	
	Non-Hispanic Black	2.10[1.70,2.50]	2.20[1.70,2.80]	2.20[1.70,2.80]		1.90[1.50,2.40]	2.00[1.60,2.50]	
	Other Race - Including Multi-Racial	2.10[1.70,2.50]	2.25[1.80,2.70]	2.20[1.70,2.70]		1.95[1.42,2.60]	1.90[1.50,2.47]	
Monocyte number(1000cells/uL)	Mexican American	0.50[0.40,0.60]	0.60[0.50,0.70]	0.50[0.40,0.60]	<0.001	0.50[0.50,0.60]	0.50[0.40,0.70]	<0.001
	Other Hispanic	0.50[0.40,0.70]	0.50[0.40,0.70]	0.60[0.50,0.70]		0.50[0.40,0.70]	0.50[0.40,0.70]	
	Non-Hispanic White	0.50[0.40,0.70]	0.60[0.50,0.70]	0.60[0.50,0.70]		0.60[0.50,0.70]	0.60[0.44,0.70]	
	Non-Hispanic Black	0.50[0.40,0.60]	0.50[0.40,0.60]	0.50[0.40,0.60]		0.50[0.40,0.60]	0.50[0.40,0.60]	
	Other Race - Including Multi-Racial	0.50[0.40,0.60]	0.50[0.40,0.60]	0.50[0.40,0.70]		0.50[0.40,0.60]	0.50[0.40,0.60]	
Segmented neutrophils num(1000 cells/uL)	Mexican American	4.20[3.30,5.30]	4.30[3.40,5.40]	4.50[3.70,5.50]	<0.001	4.30[3.50,5.30]	4.10[3.40,5.00]	<0.001
	Other Hispanic	4.10[3.30,5.20]	4.20[3.30,5.20]	4.50[3.50,5.60]		4.00[3.02,4.84]	4.10[3.30,4.70]	
	Non-Hispanic White	4.00[3.20,5.10]	4.30[3.40,5.40]	4.70[3.80,5.80]		4.50[3.63,5.40]	4.00[3.20,5.00]	
	Non-Hispanic Black	3.20[2.40,4.40]	3.30[2.40,4.50]	3.70[2.83,4.90]		3.30[2.40,4.40]	3.30[2.40,4.30]	
	Other Race - Including Multi-Racial	3.90[3.00,4.90]	3.90[3.10,5.10]	4.20[3.40,5.50]		3.80[3.08,4.83]	3.70[2.90,4.70]	
Eosinophils number(1000 cells/uL)	Mexican American	0.10[0.10,0.20]	0.20[0.10,0.30]	0.20[0.10,0.30]	<0.001	0.20[0.10,0.30]	0.20[0.10,0.20]	0.001
	Other Hispanic	0.20[0.10,0.30]	0.20[0.10,0.30]	0.20[0.10,0.30]		0.20[0.10,0.30]	0.20[0.10,0.30]	
	Non-Hispanic White	0.20[0.10,0.20]	0.20[0.10,0.30]	0.20[0.10,0.30]		0.20[0.10,0.30]	0.20[0.10,0.30]	
	Non-Hispanic Black	0.10[0.10,0.20]	0.13[0.10,0.20]	0.20[0.10,0.20]		0.20[0.10,0.20]	0.10[0.10,0.20]	
	Other Race - Including Multi-Racial	0.20[0.10,0.20]	0.20[0.10,0.30]	0.20[0.10,0.30]		0.20[0.10,0.21]	0.20[0.10,0.30]	
Basophils number(1000 cells/uL)	Mexican American	0.00[0.00,0.10]	0.00[0.00,0.10]	0.00[0.00,0.10]	<0.001	0.00[0.00,0.10]	0.00[0.00,0.10]	0.002
	Other Hispanic	0.00[0.00,0.10]	0.00[0.00,0.10]	0.00[0.00,0.10]		0.00[0.00,0.10]	0.00[0.00,0.10]	
	Non-Hispanic White	0.00[0.00,0.10]	0.10[0.00,0.10]	0.10[0.00,0.10]		0.00[0.00,0.10]	0.00[0.00,0.10]	

	Non-Hispanic Black	0.00[0.00,0.10]	0.00[0.00,0.10]	0.00[0.00,0.10]		0.00[0.00,0.10]	0.00[0.00,0.10]	
	Other Race - Including Multi-Racial	0.00[0.00,0.10]	0.00[0.00,0.10]	0.00[0.00,0.10]		0.00[0.00,0.10]	0.00[0.00,0.10]	
Red blood cell count(millioncells/uL)	Mexican American	4.79[4.43,5.14]	4.85[4.50,5.17]	4.70[4.39,5.07]		4.56[4.19,4.92]	4.57[4.28,4.90]	
	Other Hispanic	4.68[4.38,5.07]	4.76[4.48,5.09]	4.73[4.42,5.09]		4.53[4.22,4.92]	4.62[4.37,4.93]	
	Non-Hispanic White	4.70[4.39,5.04]	4.68[4.38,5.00]	4.72[4.37,5.02]	<0.001	4.51[4.11,4.86]	4.55[4.28,4.84]	0.005
	Non-Hispanic Black	4.59[4.23,4.97]	4.74[4.39,5.08]	4.60[4.26,4.99]		4.43[4.11,4.80]	4.50[4.18,4.88]	
	Other Race - Including Multi-Racial	4.74[4.40,5.09]	4.77[4.44,5.09]	4.74[4.32,5.10]		4.50[4.19,4.82]	4.52[4.20,4.84]	
Hemoglobin (g/dL)	Mexican American	14.60[13.40,15.70]	14.50[13.40,15.40]	14.20[13.10,15.30]		14.10[12.90,15.00]	14.20[13.30,15.20]	
	Other Hispanic	14.20[13.30,15.30]	14.10[13.10,15.10]	14.10[13.00,15.20]		13.80[12.76,14.70]	14.10[13.30,15.00]	
	Non-Hispanic White	14.50[13.60,15.50]	14.30[13.50,15.20]	14.40[13.30,15.20]	<0.001	14.00[12.90,15.10]	14.20[13.40,15.00]	<0.001
	Non-Hispanic Black	13.50[12.50,14.70]	13.60[12.60,14.60]	13.20[12.20,14.30]		12.80[12.00,13.93]	13.30[12.50,14.10]	
	Other Race - Including Multi-Racial	14.30[13.20,15.40]	14.10[13.20,15.10]	14.10[12.90,15.30]		13.60[12.68,14.30]	13.90[13.10,14.90]	
Hematocrit (%)	Mexican American	42.80[39.10,46.10]	42.80[39.40,45.30]	41.80[38.49,45.20]		41.80[38.35,44.60]	41.60[38.80,44.90]	
	Other Hispanic	41.80[38.80,45.20]	42.05[38.80,44.90]	41.80[38.10,44.40]		40.67[37.80,43.60]	41.69[39.78,44.23]	
	Non-Hispanic White	42.60[39.70,45.40]	42.20[39.50,45.10]	42.10[38.90,44.70]	<0.001	41.60[38.02,44.88]	41.70[39.20,44.30]	<0.001
	Non-Hispanic Black	40.39[37.10,43.98]	40.90[37.80,43.90]	39.50[36.60,42.50]		39.80[36.50,42.79]	39.80[37.40,42.40]	
	Other Race - Including Multi-Racial	42.20[38.80,45.40]	41.80[38.67,44.99]	41.69[37.63,44.90]		40.59[38.87,42.65]	41.55[37.23,43.97]	
Mean cell volume(fL)	Mexican American	89.40[86.60,92.00]	88.30[84.80,91.10]	88.90[86.10,91.90]		91.00[87.90,94.10]	91.59[88.70,94.60]	
	Other Hispanic	89.30[86.20,92.40]	88.10[84.60,91.40]	88.10[85.50,91.40]		90.40[86.90,93.66]	90.60[87.10,92.80]	
	Non-Hispanic White	90.60[87.80,93.30]	90.50[87.40,93.20]	89.60[86.60,92.64]	<0.001	92.60[88.90,95.50]	91.90[89.10,94.60]	<0.001
	Non-Hispanic Black	88.80[84.50,92.50]	86.70[82.70,90.60]	86.90[82.46,90.60]		88.90[84.40,92.60]	88.86[84.40,92.60]	
	Other Race - Including Multi-Racial	89.40[86.40,92.40]	88.90[84.80,91.60]	88.70[84.60,91.90]		90.70[87.72,93.11]	91.40[87.96,94.60]	
Mean cell hemoglobin(pg)	Mexican American	30.50[29.40,31.50]	29.90[28.60,31.10]	30.30[29.00,31.30]		30.90[29.80,32.00]	31.20[30.10,32.50]	
	Other Hispanic	30.40[29.20,31.50]	29.80[28.40,31.00]	29.90[28.70,31.20]	<0.001	30.60[29.20,31.70]	30.70[29.58,31.70]	<0.001
	Non-Hispanic White	30.90[29.90,32.00]	30.70[29.60,31.80]	30.50[29.30,31.60]		31.20[29.83,32.59]	31.30[30.20,32.30]	

	Non-Hispanic Black	29.80[28.00,31.30]	28.90[27.20,30.40]	29.00[27.19,30.30]		29.50[27.70,30.90]	29.80[28.00,31.20]	
	Other Race - Including Multi-Racial	30.40[29.10,31.50]	30.10[28.50,31.18]	29.90[28.60,31.30]		30.42[29.51,31.50]	31.10[29.78,32.30]	
Mean Cell Hgb Conc.(g/dL)	Mexican American	34.00[33.50,34.70]	33.80[33.20,34.40]	33.90[33.30,34.50]	<0.001	33.90[33.30,34.50]	34.10[33.60,34.60]	<0.001
	Other Hispanic	34.00[33.40,34.50]	33.70[33.20,34.20]	33.80[33.30,34.50]		33.80[33.20,34.30]	33.82[33.40,34.37]	
	Non-Hispanic White	34.10[33.60,34.70]	33.90[33.40,34.50]	33.90[33.30,34.50]		33.80[33.30,34.34]	34.00[33.50,34.60]	
	Non-Hispanic Black	33.40[32.80,34.00]	33.30[32.60,33.80]	33.20[32.50,33.80]		33.00[32.50,33.70]	33.40[32.80,34.00]	
	Other Race - Including Multi-Racial	33.90[33.30,34.50]	33.65[33.00,34.30]	33.80[33.10,34.30]		33.60[33.10,34.13]	34.00[33.30,34.60]	
Red cell distribution width(%)	Mexican American	12.70[12.20,13.30]	13.10[12.50,13.80]	13.00[12.40,13.80]	<0.001	13.10[12.50,13.80]	13.10[12.44,13.60]	<0.001
	Other Hispanic	12.70[12.30,13.40]	13.28[12.60,13.90]	13.10[12.50,13.80]		13.10[12.60,13.80]	13.00[12.50,13.70]	
	Non-Hispanic White	12.60[12.10,13.10]	13.10[12.50,13.70]	13.20[12.50,13.90]		13.10[12.50,13.90]	12.90[12.40,13.60]	
	Non-Hispanic Black	13.05[12.40,13.90]	13.70[13.00,14.50]	13.80[13.00,14.70]		13.70[13.00,14.58]	13.70[12.90,14.40]	
	Other Race - Including Multi-Racial	12.70[12.20,13.40]	13.10[12.50,13.90]	13.10[12.50,13.90]		13.00[12.55,13.70]	12.93[12.40,13.79]	
Platelet count(1000cells/uL)	Mexican American	253.00[217.00,296.00]	254.00[214.00,300.59]	240.00[202.00,285.67]	<0.001	239.00[204.90,275.53]	232.00[201.00,271.00]	0.374
	Other Hispanic	254.00[215.00,297.82]	253.00[216.90,296.00]	255.00[214.00,311.00]		243.00[191.05,289.72]	239.00[201.36,276.88]	
	Non-Hispanic White	245.00[210.00,287.00]	249.00[210.00,294.00]	234.00[195.00,285.23]		229.00[187.00,284.00]	231.00[195.00,273.00]	
	Non-Hispanic Black	250.00[210.00,295.00]	247.00[209.00,296.00]	252.00[210.00,305.67]		226.77[192.00,266.00]	231.00[194.00,276.00]	
	Other Race - Including Multi-Racial	245.00[211.00,289.00]	249.00[210.00,296.62]	241.41[202.82,292.00]		207.00[195.00,261.77]	226.00[192.00,253.38]	
Mean platelet volume(fL)	Mexican American	8.20[7.70,8.80]	8.20[7.60,8.90]	8.40[7.80,9.00]	<0.001	8.50[7.90,9.10]	8.30[7.90,9.00]	<0.001
	Other Hispanic	8.20[7.60,8.90]	8.20[7.70,8.80]	8.40[7.90,9.00]		8.40[7.80,9.10]	8.60[8.10,9.10]	
	Non-Hispanic White	8.10[7.50,8.60]	8.10[7.50,8.70]	8.20[7.60,8.80]		8.17[7.60,8.80]	8.20[7.60,8.90]	
	Non-Hispanic Black	8.20[7.60,8.90]	8.20[7.60,8.90]	8.30[7.80,9.00]		8.60[8.00,9.10]	8.40[7.80,9.07]	
	Other Race - Including Multi-Racial	8.00[7.50,8.60]	8.00[7.40,8.60]	8.00[7.50,8.60]		8.60[7.50,9.29]	8.20[7.60,8.77]	
Folate, RBC (nmol/L RBC)	Mexican American	772.40[545.90,1052.46]	873.67[657.00,1130.00]	974.00[703.13,1260.00]	<0.001	882.66[639.85,1230.00]	983.07[714.42,1240.00]	<0.001
	Other Hispanic	779.00[564.00,1040.00]	882.87[631.90,1162.38]	934.68[695.99,1270.00]		894.77[585.80,1110.00]	913.00[682.77,1260.00]	
	Non-Hispanic White	869.80[620.60,1220.00]	1050.00[736.10,1480.00]	1120.00[788.20,1600.00]		922.94[616.09,1349.88]	1080.29[783.70,1560.00]	

	Non-Hispanic Black	638.70[459.80,914.00]	728.35[528.80,1020.00]	840.00[594.25,1209.73]		728.36[534.26,1071.35]	879.40[629.33,1300.00]	
	Other Race - Including Multi-Racial	815.00[584.19,1110.00]	920.00[627.32,1271.41]	1000.00[704.27,1437.15]		797.30[542.74,1052.26]	1021.85[769.75,1490.00]	
Folate, serum(nmol/L)	Mexican American	25.60[18.60,35.60]	27.90[20.24,38.40]	30.40[22.35,41.74]	<0.001	34.80[23.10,43.31]	34.00[25.40,43.13]	<0.001
	Other Hispanic	27.99[20.60,37.80]	29.90[20.56,41.00]	29.69[24.13,40.30]		29.94[24.50,40.01]	31.97[22.75,42.85]	
	Non-Hispanic White	31.40[22.00,44.40]	36.97[23.80,56.20]	36.04[24.76,55.52]		37.42[24.37,56.22]	41.40[28.10,58.21]	
	Non-Hispanic Black	23.31[16.55,32.40]	24.50[17.90,35.60]	27.40[19.60,40.77]		25.63[17.07,38.95]	29.33[21.67,42.26]	
	Other Race - Including Multi-Racial	27.56[19.38,38.40]	29.14[22.20,43.66]	39.60[25.10,59.53]		29.40[18.40,46.08]	37.71[30.70,48.49]	
Vitamin B12(pmol/L)	Mexican American	357.20[278.96,470.10]	370.17[284.13,466.33]	378.59[288.70,512.42]	<0.001	384.63[278.80,586.27]	374.42[266.40,493.69]	<0.001
	Other Hispanic	347.40[259.80,451.67]	323.07[255.82,474.81]	369.86[280.98,476.73]		335.64[228.96,471.43]	344.43[265.76,504.70]	
	Non-Hispanic White	340.96[259.04,452.40]	358.19[262.73,479.78]	343.91[261.26,496.91]		353.57[244.28,511.96]	374.90[275.30,520.64]	
	Non-Hispanic Black	357.20[278.96,470.10]	370.17[284.13,466.33]	378.59[288.70,512.42]		399.28[285.89,557.51]	423.60[304.29,614.86]	
	Other Race - Including Multi-Racial	366.05[270.10,485.60]	377.12[263.11,492.06]	398.40[267.41,532.90]		487.56[321.42,618.92]	440.57[276.80,621.36]	
Homocysteine(umol/L)	Mexican American	6.81[5.70,8.21]	7.36[6.12,8.75]	7.54[6.17,9.52]	<0.001	9.11[7.20,11.22]	8.79[7.08,10.99]	<0.001
	Other Hispanic	6.97[5.92,8.66]	8.04[6.48,10.30]	8.35[6.71,9.90]		9.42[7.79,11.47]	9.04[7.79,10.62]	
	Non-Hispanic White	7.88[6.51,9.51]	8.80[7.31,10.80]	8.99[7.31,11.18]		10.75[8.04,14.16]	9.08[7.52,11.10]	
	Non-Hispanic Black	7.64[6.27,9.31]	8.26[6.84,9.98]	8.87[6.95,11.42]		10.70[8.20,13.77]	9.08[7.51,11.19]	
	Other Race - Including Multi-Racial	7.26[6.01,8.84]	7.90[6.59,9.93]	8.05[6.05,10.23]		8.27[6.40,11.00]	7.99[6.90,10.51]	
Blood mercury, total(nmol/L)	Mexican American	3.49[2.00,5.99]	3.39[1.90,5.80]	2.99[1.70,5.40]	<0.001	1.83[0.85,3.52]	2.29[1.29,4.60]	<0.001
	Other Hispanic	5.20[2.81,9.80]	4.99[3.00,8.50]	4.80[2.50,9.42]		6.50[3.34,9.09]	6.92[3.64,12.57]	
	Non-Hispanic White	4.40[2.20,8.98]	4.54[2.30,8.70]	3.74[2.00,7.10]		2.50[1.14,4.50]	5.00[2.70,10.42]	
	Non-Hispanic Black	4.50[2.50,8.38]	4.90[2.70,9.20]	5.19[2.90,9.20]		3.60[2.05,7.30]	4.77[2.62,8.41]	
	Other Race - Including Multi-Racial	7.56[2.99,17.35]	8.63[2.84,21.11]	6.56[2.47,16.70]		15.60[5.78,24.59]	6.52[3.23,18.02]	
Mercury, inorganic(nmol/L)	Mexican American	1.25[1.25,1.50]	1.25[0.95,1.40]	1.25[0.95,1.50]	<0.001	0.95[0.95,0.95]	0.95[0.95,0.95]	0.047
	Other Hispanic	1.25[0.95,1.50]	1.25[0.95,1.50]	1.25[0.95,1.50]		0.95[0.95,2.00]	0.95[0.95,1.60]	
	Non-Hispanic White	1.25[1.25,1.50]	1.25[0.95,1.50]	1.25[0.95,1.50]		0.95[0.95,0.95]	0.95[0.95,1.75]	

	Non-Hispanic Black	1.25[1.25,1.50]	1.25[0.95,1.50]	1.25[0.95,1.50]		0.95[0.95,0.95]	0.95[0.95,1.50]	
	Other Race - Including Multi-Racial	1.25[0.95,1.50]	1.25[0.95,1.60]	1.25[0.95,1.50]		1.18[0.95,2.34]	0.95[0.95,1.61]	
Tot Iron Binding Capacity TIBC(umol/L)	Mexican American	63.94[57.46,71.60]	63.55[55.85,69.12]	61.78[56.92,70.10]	<0.001	63.19[56.92,69.63]	63.66[57.26,69.87]	<0.001
	Other Hispanic	62.50[55.89,70.88]	60.54[55.85,68.31]	63.11[55.70,70.29]		60.49[57.27,65.38]	63.64[54.30,68.94]	
	Non-Hispanic White	62.65[56.24,69.99]	61.34[55.99,67.84]	61.76[55.40,68.56]		63.82[56.21,71.85]	64.08[57.46,70.71]	
	Non-Hispanic Black	61.38[54.80,69.81]	59.25[52.66,65.34]	58.49[51.91,64.98]		59.99[52.65,65.24]	58.89[52.98,65.69]	
	Other Race - Including Multi-Racial	62.47[56.06,68.75]	60.54[54.09,67.85]	62.29[55.39,69.09]		60.58[52.92,62.74]	61.39[56.21,69.38]	
Ferritin(ug/L)	Mexican American	52.00[24.00,114.00]	84.22[28.00,186.00]	90.27[37.96,197.28]	<0.001	92.41[53.00,169.10]	110.51[69.00,186.33]	0.011
	Other Hispanic	54.14[27.00,109.00]	92.26[40.78,164.63]	96.34[39.86,214.78]		91.11[49.51,140.37]	80.37[54.56,169.00]	
	Non-Hispanic White	68.00[33.00,132.00]	93.20[48.48,169.00]	112.13[57.00,212.96]		104.00[54.00,193.21]	101.00[54.00,182.00]	
	Non-Hispanic Black	58.00[23.00,131.00]	86.07[36.00,164.00]	110.84[48.08,226.00]		151.00[81.85,237.40]	133.00[76.32,227.57]	
	Other Race - Including Multi-Racial	66.00[31.00,145.00]	95.36[38.00,177.90]	105.85[51.74,267.93]		155.36[103.32,235.39]	123.96[68.94,276.12]	
Cotinine, Serum (ng/mL)	Mexican American	0.04[0.01,0.48]	0.03[0.01,0.23]	0.03[0.01,0.21]	<0.001	0.04[0.01,0.35]	0.02[0.01,0.07]	<0.001
	Other Hispanic	0.04[0.01,1.80]	0.04[0.01,0.41]	0.03[0.01,0.18]		0.04[0.02,0.19]	0.04[0.01,0.42]	
	Non-Hispanic White	0.05[0.01,40.40]	0.04[0.01,57.63]	0.04[0.01,0.60]		0.04[0.02,0.47]	0.03[0.01,0.09]	
	Non-Hispanic Black	0.37[0.04,110.00]	0.20[0.03,115.87]	0.10[0.03,25.88]		0.10[0.04,2.58]	0.06[0.02,1.50]	
	Other Race - Including Multi-Racial	0.05[0.02,4.90]	0.04[0.02,0.71]	0.04[0.02,0.60]		0.03[0.02,0.06]	0.04[0.02,0.22]	
gamma-tocopherol (umol/L)	Mexican American	4.56[3.29,6.20]	5.24[3.54,7.33]	5.63[3.73,8.42]	<0.001	5.23[3.50,7.43]	5.66[3.23,8.10]	<0.001
	Other Hispanic	4.22[3.00,5.65]	4.71[3.24,6.98]	4.64[3.41,6.17]		3.77[2.55,5.51]	3.76[2.09,4.73]	
	Non-Hispanic White	4.59[2.93,6.53]	5.07[3.19,7.49]	5.38[3.39,8.11]		4.46[2.69,7.18]	4.35[2.29,7.03]	
	Non-Hispanic Black	5.02[3.64,6.82]	5.38[3.72,7.35]	6.41[4.39,8.39]		7.62[4.35,10.11]	5.83[3.48,7.71]	
	Other Race - Including Multi-Racial	4.61[3.18,6.08]	4.40[3.05,6.34]	4.71[2.98,7.23]		3.88[2.76,4.12]	3.98[1.93,7.60]	
Retinyl palmitate (umol/L)	Mexican American	0.04[0.03,0.07]	0.03[0.03,0.07]	0.04[0.03,0.08]	<0.001	0.05[0.02,0.08]	0.06[0.03,0.09]	<0.001
	Other Hispanic	0.04[0.03,0.07]	0.04[0.03,0.07]	0.06[0.03,0.09]		0.05[0.04,0.07]	0.04[0.03,0.07]	
	Non-Hispanic White	0.05[0.03,0.09]	0.05[0.03,0.09]	0.06[0.03,0.10]		0.05[0.03,0.09]	0.07[0.04,0.11]	

	Non-Hispanic Black	0.05[0.03,0.08]	0.05[0.03,0.08]	0.05[0.03,0.09]		0.05[0.03,0.08]	0.07[0.04,0.11]	
	Other Race - Including Multi-Racial	0.04[0.03,0.07]	0.05[0.03,0.09]	0.05[0.03,0.10]		0.05[0.02,0.09]	0.08[0.05,0.12]	
Retinyl stearate (umol/L)	Mexican American	0.02[0.01,0.02]	0.02[0.01,0.02]	0.02[0.01,0.02]	<0.001	0.01[0.01,0.01]	0.01[0.01,0.01]	0.002
	Other Hispanic	0.01[0.01,0.02]	0.02[0.01,0.02]	0.02[0.01,0.02]		0.01[0.01,0.01]	0.01[0.01,0.01]	
	Non-Hispanic White	0.02[0.01,0.02]	0.02[0.01,0.02]	0.02[0.01,0.02]		0.01[0.01,0.03]	0.01[0.01,0.02]	
	Non-Hispanic Black	0.01[0.01,0.02]	0.02[0.01,0.02]	0.02[0.01,0.02]		0.01[0.01,0.01]	0.01[0.01,0.01]	
	Other Race - Including Multi-Racial	0.02[0.01,0.02]	0.02[0.02,0.02]	0.02[0.01,0.02]		0.01[0.01,0.01]	0.01[0.01,0.02]	
Retinol (umol/L)	Mexican American	1.76[1.47,2.11]	1.80[1.46,2.10]	1.81[1.46,2.12]	<0.001	1.85[1.55,2.29]	2.07[1.72,2.48]	<0.001
	Other Hispanic	1.82[1.50,2.16]	1.86[1.57,2.26]	1.91[1.50,2.35]		1.97[1.68,2.31]	1.89[1.69,2.39]	
	Non-Hispanic White	2.06[1.72,2.46]	2.08[1.74,2.48]	2.16[1.76,2.59]		2.21[1.79,2.59]	2.31[1.98,2.70]	
	Non-Hispanic Black	1.69[1.37,2.05]	1.78[1.42,2.18]	1.94[1.56,2.39]		2.10[1.68,2.63]	2.06[1.66,2.40]	
	Other Race - Including Multi-Racial	1.82[1.49,2.18]	1.95[1.63,2.24]	2.05[1.73,2.45]		2.25[1.62,2.69]	2.28[1.80,2.61]	
Albumin, urine(ug/mL)	Mexican American	7.50[4.20,13.80]	8.37[4.40,17.30]	15.20[6.30,52.84]	<0.001	10.67[5.50,27.11]	8.00[4.00,19.20]	<0.001
	Other Hispanic	7.40[3.90,13.60]	8.09[4.10,17.10]	15.74[6.70,44.99]		12.97[5.80,28.28]	9.03[4.87,17.91]	
	Non-Hispanic White	6.30[3.30,11.80]	7.50[4.00,14.90]	12.00[5.30,31.00]		16.80[6.40,43.16]	7.70[3.70,16.07]	
	Non-Hispanic Black	9.20[5.15,18.40]	9.55[5.30,19.50]	16.23[7.40,48.84]		17.20[7.60,53.32]	10.80[5.10,28.37]	
	Other Race - Including Multi-Racial	6.30[3.20,12.10]	6.79[3.50,12.90]	11.20[5.25,45.04]		9.60[4.01,24.79]	7.09[4.20,14.88]	
Albumin (g/L)	Mexican American	44.00[41.00,46.00]	42.00[40.00,44.00]	42.00[39.00,44.00]	<0.001	42.00[40.00,45.00]	43.00[41.00,45.00]	<0.001
	Other Hispanic	43.00[41.00,46.00]	42.00[40.00,44.00]	42.00[39.00,44.00]		43.00[41.00,45.00]	42.00[40.98,44.00]	
	Non-Hispanic White	44.00[41.00,46.00]	42.00[40.00,44.00]	42.00[40.00,44.00]		42.00[40.00,44.00]	43.00[41.00,44.00]	
	Non-Hispanic Black	42.00[40.00,45.00]	41.00[39.00,44.00]	41.00[38.00,43.00]		42.00[40.00,44.00]	42.00[39.15,43.00]	
	Other Race - Including Multi-Racial	44.00[41.00,46.00]	43.00[41.00,45.00]	42.00[40.00,44.00]		43.00[41.61,44.00]	43.00[41.00,45.00]	
Creatinine, urine(mg/dL)	Mexican American	122.00[72.00,177.00]	117.00[66.00,168.00]	97.00[60.00,146.00]	<0.001	91.67[55.00,137.06]	95.00[53.12,130.44]	<0.001
	Other Hispanic	124.00[72.00,181.00]	110.83[63.00,169.13]	101.00[63.00,153.00]		105.54[62.00,156.90]	101.00[68.50,144.66]	
	Non-Hispanic White	107.00[57.00,166.00]	100.00[56.00,153.00]	101.00[62.00,149.00]		94.00[53.17,140.00]	91.00[49.00,138.50]	

	Non-Hispanic Black	163.00[105.00,235.00]	152.00[98.00,218.08]	125.00[82.00,184.00]		125.00[83.06,192.47]	119.00[76.09,177.00]	
	Other Race - Including Multi-Racial	100.00[52.00,168.00]	86.51[49.00,144.00]	91.28[50.00,140.00]		79.58[40.40,99.88]	75.14[40.23,125.08]	
Creatinine(umol/L)	Mexican American	65.42[54.81,79.56]	68.07[55.69,79.56]	64.53[53.04,79.56]	<0.001	70.70[57.81,85.65]	70.72[59.23,83.10]	<0.001
	Other Hispanic	68.95[56.58,79.60]	70.72[60.11,83.10]	70.72[56.58,82.21]		70.72[61.89,88.40]	70.70[57.46,83.05]	
	Non-Hispanic White	75.14[62.76,88.40]	77.79[66.30,88.40]	79.56[65.42,94.59]		81.33[69.76,105.24]	79.56[64.53,92.82]	
	Non-Hispanic Black	77.79[63.65,90.17]	81.33[69.84,97.24]	81.33[67.18,100.78]		90.17[73.37,113.13]	82.21[70.71,100.22]	
	Other Race - Including Multi-Racial	70.72[58.34,82.21]	70.72[61.00,85.75]	71.82[59.92,89.28]		86.33[61.88,97.23]	73.37[61.88,88.40]	
Alanine Aminotransferase (ALT) (U/L)	Mexican American	22.00[17.00,32.00]	26.00[19.00,39.00]	25.00[19.00,37.00]	<0.001	19.00[16.00,26.00]	21.00[17.00,29.00]	<0.001
	Other Hispanic	21.00[16.00,30.00]	24.00[18.00,33.00]	24.00[18.00,33.00]		20.00[16.00,24.00]	20.00[17.00,25.54]	
	Non-Hispanic White	21.00[16.00,28.00]	22.00[17.00,29.00]	23.00[18.00,31.00]		18.00[15.00,23.00]	20.00[17.00,25.00]	
	Non-Hispanic Black	18.00[14.00,24.00]	20.00[15.00,27.00]	19.00[15.00,26.00]		18.00[14.00,24.00]	19.00[15.00,24.00]	
	Other Race - Including Multi-Racial	19.00[15.00,27.00]	22.00[17.00,31.00]	23.00[17.31,33.00]		16.70[14.65,25.00]	21.16[17.00,26.00]	
Aspartate Aminotransferase (AST) (U/L)	Mexican American	23.00[19.00,28.00]	25.00[21.00,31.00]	23.00[19.00,30.00]	<0.001	22.00[19.00,27.00]	23.00[19.00,28.00]	0.018
	Other Hispanic	22.00[18.00,27.00]	24.00[20.00,29.00]	23.00[19.00,29.00]		22.00[19.00,25.32]	22.00[19.00,27.00]	
	Non-Hispanic White	22.00[19.00,27.00]	23.00[20.00,27.00]	23.00[19.00,28.00]		23.00[20.00,28.00]	23.00[20.00,27.00]	
	Non-Hispanic Black	22.00[18.00,26.00]	22.00[19.00,28.00]	21.00[17.00,26.00]		22.00[19.00,27.00]	22.00[19.00,26.00]	
	Other Race - Including Multi-Racial	22.00[18.00,26.00]	23.00[19.00,27.00]	24.00[19.00,29.94]		25.00[20.00,27.00]	24.00[21.00,29.00]	
Alkaline Phosphatase (ALP) (U/L)	Mexican American	72.00[59.00,86.00]	77.00[63.00,93.00]	79.00[64.00,98.00]	<0.001	82.00[68.00,98.80]	70.00[59.00,88.00]	<0.001
	Other Hispanic	69.00[56.73,82.00]	76.00[63.00,89.00]	80.00[62.00,98.00]		78.07[66.00,92.00]	73.48[61.57,85.84]	
	Non-Hispanic White	64.00[52.00,77.00]	69.00[57.00,83.00]	69.00[56.00,86.00]		76.00[58.15,94.74]	66.00[54.00,80.00]	
	Non-Hispanic Black	64.00[52.00,79.00]	68.00[56.00,84.00]	74.00[60.00,91.00]		75.00[61.00,97.09]	71.00[58.00,86.27]	
	Other Race - Including Multi-Racial	62.00[51.00,77.00]	66.00[54.00,81.00]	68.00[54.00,87.00]		66.93[51.59,85.00]	66.00[52.57,84.00]	
Blood urea nitrogen (mmol/L)	Mexican American	4.28[3.21,5.00]	4.64[3.57,5.71]	4.64[3.93,6.07]	<0.001	5.40[4.28,6.80]	5.00[4.28,6.10]	<0.001
	Other Hispanic	4.28[3.57,5.36]	4.64[3.93,5.71]	4.64[3.93,6.07]		5.37[4.60,6.43]	5.25[4.28,6.43]	
	Non-Hispanic White	4.64[3.57,5.71]	5.36[4.28,6.43]	5.70[4.28,7.14]		6.07[4.60,7.50]	5.70[4.60,6.78]	

	Non-Hispanic Black	3.73[2.86,4.64]	4.28[3.21,5.36]	4.64[3.57,6.07]		5.40[4.30,7.50]	4.64[3.93,6.07]	
	Other Race - Including Multi-Racial	4.28[3.21,5.36]	4.64[3.93,5.71]	5.00[3.93,6.43]		5.67[4.28,7.13]	5.00[3.93,6.10]	
Total Calcium (mmol/L)	Mexican American	2.35[2.28,2.40]	2.33[2.28,2.38]	2.33[2.28,2.40]	<0.001	2.33[2.28,2.38]	2.35[2.30,2.40]	0.002
	Other Hispanic	2.35[2.30,2.40]	2.35[2.30,2.40]	2.35[2.30,2.42]		2.38[2.30,2.42]	2.35[2.28,2.41]	
	Non-Hispanic White	2.35[2.30,2.42]	2.35[2.30,2.40]	2.35[2.30,2.42]		2.38[2.30,2.42]	2.35[2.30,2.42]	
	Non-Hispanic Black	2.35[2.30,2.42]	2.35[2.30,2.42]	2.38[2.30,2.42]		2.38[2.30,2.45]	2.38[2.33,2.42]	
	Other Race - Including Multi-Racial	2.35[2.28,2.40]	2.35[2.28,2.40]	2.35[2.30,2.42]		2.35[2.27,2.42]	2.35[2.30,2.42]	
Bicarbonate (mmol/L)	Mexican American	24.00[23.00,26.00]	25.00[23.00,26.00]	25.00[23.00,26.00]	<0.001	25.00[23.00,26.00]	25.00[23.00,26.00]	<0.001
	Other Hispanic	25.00[23.00,26.00]	25.00[23.00,26.00]	25.00[23.00,27.00]		25.00[23.00,26.81]	24.00[23.00,26.00]	
	Non-Hispanic White	25.00[23.00,26.00]	25.00[24.00,27.00]	25.00[23.00,26.00]		25.00[23.00,26.00]	25.00[24.00,27.00]	
	Non-Hispanic Black	25.00[23.00,26.00]	25.00[24.00,27.00]	25.00[23.00,27.00]		25.00[23.00,27.00]	26.00[24.00,27.00]	
	Other Race - Including Multi-Racial	25.00[23.00,26.00]	25.00[24.00,27.00]	25.00[23.00,26.00]		25.00[24.00,26.27]	26.00[25.00,27.00]	
Gamma Glutamyl Transferase (GGT) (U/L)	Mexican American	20.00[14.00,31.00]	25.00[17.00,40.00]	27.00[19.00,42.00]	<0.001	21.00[15.00,31.00]	21.00[16.00,32.00]	<0.001
	Other Hispanic	19.00[13.00,29.00]	25.00[17.00,37.00]	28.00[18.00,42.95]		22.00[15.00,34.02]	22.00[15.00,31.00]	
	Non-Hispanic White	18.00[13.00,27.00]	21.00[15.00,31.00]	24.00[17.00,39.00]		19.00[14.00,32.00]	19.00[14.00,27.00]	
	Non-Hispanic Black	20.00[14.00,29.00]	24.00[17.00,35.00]	26.00[19.00,39.00]		23.00[17.00,35.66]	23.00[17.00,32.00]	
	Other Race - Including Multi-Racial	17.00[12.00,25.00]	22.00[16.00,31.00]	25.00[18.00,39.51]		21.61[16.00,32.00]	20.00[15.00,31.00]	
Iron (umol/L)	Mexican American	15.40[11.28,20.40]	14.10[10.40,18.63]	14.00[10.60,18.30]	<0.001	13.80[10.78,17.90]	15.79[12.36,19.90]	<0.001
	Other Hispanic	14.90[10.93,19.50]	13.80[10.60,17.90]	13.49[10.68,18.09]		14.04[10.92,18.35]	13.95[10.57,18.30]	
	Non-Hispanic White	15.80[12.00,20.20]	14.50[11.10,18.30]	13.61[10.70,17.70]		14.33[10.68,18.44]	15.22[11.82,19.00]	
	Non-Hispanic Black	13.40[9.70,17.60]	12.50[9.50,15.90]	11.60[9.13,14.90]		12.09[9.50,15.60]	12.54[9.90,15.80]	
	Other Race - Including Multi-Racial	15.80[12.00,20.10]	14.50[10.70,18.43]	14.15[10.90,17.71]		12.90[10.26,17.91]	14.69[11.50,18.42]	
Lactate Dehydrogenase (LDH) (U/L)	Mexican American	125.00[111.00,144.00]	133.00[116.97,150.00]	128.00[112.00,148.00]	<0.001	138.00[119.00,155.00]	128.00[112.00,147.00]	<0.001
	Other Hispanic	126.00[111.00,144.00]	135.00[118.01,156.00]	130.00[114.00,152.00]		135.00[121.00,158.00]	131.00[115.82,152.55]	
	Non-Hispanic White	127.00[112.00,144.00]	135.00[120.00,155.00]	133.00[117.00,154.00]		144.00[125.00,169.00]	134.00[119.00,152.00]	

	Non-Hispanic Black	131.00[114.00,151.00]	140.00[122.00,161.00]	141.00[121.99,162.00]		150.68[131.00,169.17]	141.00[123.00,160.82]	
	Other Race - Including Multi-Racial	123.00[110.00,142.00]	135.00[118.00,155.00]	133.00[115.75,157.00]		139.78[115.04,155.66]	131.00[115.00,150.00]	
Phosphorus (mmol/L)	Mexican American	1.20[1.07,1.32]	1.20[1.07,1.29]	1.20[1.07,1.32]	0.058	1.19[1.07,1.29]	1.19[1.07,1.29]	0.12
	Other Hispanic	1.20[1.10,1.29]	1.20[1.10,1.32]	1.20[1.10,1.32]		1.16[1.06,1.29]	1.20[1.03,1.31]	
	Non-Hispanic White	1.20[1.10,1.32]	1.20[1.10,1.32]	1.20[1.07,1.32]		1.13[1.03,1.26]	1.16[1.07,1.29]	
	Non-Hispanic Black	1.20[1.10,1.32]	1.20[1.07,1.29]	1.20[1.07,1.29]		1.14[1.07,1.29]	1.16[1.07,1.29]	
	Other Race - Including Multi-Racial	1.20[1.10,1.32]	1.20[1.07,1.32]	1.20[1.07,1.32]		1.26[1.13,1.31]	1.23[1.10,1.33]	
Bilirubin,total(umol/L)	Mexican American	10.26[8.55,13.68]	10.26[6.84,11.97]	10.26[6.84,13.68]	<0.001	10.26[8.55,11.97]	10.26[8.55,13.68]	<0.001
	Other Hispanic	10.26[6.84,13.68]	10.26[6.84,11.97]	10.26[6.84,11.97]		10.26[8.55,13.68]	10.26[8.55,11.98]	
	Non-Hispanic White	11.97[8.55,15.39]	10.26[8.55,13.68]	10.26[8.55,13.68]		10.30[8.57,13.68]	10.30[8.55,13.68]	
	Non-Hispanic Black	10.26[8.55,13.68]	10.26[6.84,11.97]	8.55[6.84,11.97]		10.26[6.84,11.97]	10.26[8.55,11.97]	
	Other Race - Including Multi-Racial	10.26[8.55,13.68]	10.26[6.84,11.97]	10.26[6.84,13.68]		10.26[8.55,13.68]	11.97[8.60,13.68]	
Protein,total(g/L)	Mexican American	73.00[70.00,76.00]	73.00[70.00,76.00]	73.00[70.00,76.00]	<0.001	74.00[70.00,77.00]	72.00[69.00,75.00]	<0.001
	Other Hispanic	73.00[70.00,76.00]	73.00[70.00,76.00]	73.00[70.00,76.00]		74.91[70.87,78.00]	73.00[70.00,76.00]	
	Non-Hispanic White	71.00[68.00,74.00]	70.00[68.00,73.00]	70.00[67.00,73.00]		72.00[68.00,76.00]	70.00[67.00,74.00]	
	Non-Hispanic Black	73.00[70.00,77.00]	73.00[70.00,76.00]	73.00[70.00,76.00]		74.00[71.00,78.00]	73.00[70.00,76.00]	
	Other Race - Including Multi-Racial	73.00[70.00,76.00]	72.00[69.00,75.00]	72.00[69.00,75.00]		76.00[73.32,79.00]	72.00[69.00,76.00]	
Uric acid(umol/L)	Mexican American	303.30[243.90,362.80]	327.10[267.70,380.70]	298.91[243.90,356.90]	<0.001	309.30[255.80,368.80]	309.30[261.70,362.80]	<0.001
	Other Hispanic	297.40[243.90,356.90]	327.10[273.60,380.70]	303.30[243.90,362.80]		309.30[262.28,362.80]	313.40[272.56,364.75]	
	Non-Hispanic White	309.30[255.80,368.80]	333.10[279.60,386.60]	333.10[273.60,398.50]		333.10[273.60,398.50]	327.10[273.60,386.60]	
	Non-Hispanic Black	297.40[243.90,356.90]	339.00[285.50,404.50]	339.00[279.60,410.40]		368.29[303.30,434.20]	350.90[291.50,410.40]	
	Other Race - Including Multi-Racial	309.30[255.80,368.80]	327.10[267.70,386.60]	321.20[273.60,392.60]		363.09[291.48,434.20]	322.35[261.70,392.60]	
Sodium(mmol/L)	Mexican American	139.00[138.00,141.00]	139.00[138.00,141.00]	138.00[137.00,140.00]	<0.001	139.50[137.00,141.00]	140.00[138.00,141.00]	0.037
	Other Hispanic	139.00[138.00,140.20]	139.00[138.00,141.00]	138.00[136.28,140.00]		139.00[138.00,141.00]	140.00[138.00,141.00]	
	Non-Hispanic White	139.00[138.00,141.00]	139.40[138.00,141.00]	139.00[137.00,141.00]		140.00[138.00,141.00]	140.00[138.00,141.00]	

	Non-Hispanic Black	139.00[138.00,141.00]	140.00[138.00,141.00]	139.00[137.00,141.00]		140.00[138.30,142.00]	140.00[138.00,141.00]	
	Other Race - Including Multi-Racial	139.00[138.00,141.00]	139.00[138.00,141.00]	139.00[137.00,141.00]		139.87[137.00,141.46]	140.00[138.00,141.00]	
Potassium(mmol/L)	Mexican American	3.90[3.70,4.10]	3.99[3.80,4.18]	4.00[3.80,4.20]	<0.001	4.10[3.90,4.38]	4.10[3.89,4.30]	<0.001
	Other Hispanic	3.90[3.80,4.10]	4.00[3.80,4.20]	4.00[3.80,4.20]		4.05[3.84,4.29]	4.00[3.80,4.19]	
	Non-Hispanic White	4.00[3.80,4.20]	4.10[3.90,4.30]	4.10[3.90,4.30]		4.20[3.90,4.43]	4.10[3.90,4.33]	
	Non-Hispanic Black	3.90[3.70,4.10]	3.92[3.70,4.18]	4.00[3.73,4.20]		4.10[3.76,4.31]	4.00[3.70,4.20]	
	Other Race - Including Multi-Racial	3.90[3.70,4.10]	3.99[3.80,4.20]	4.10[3.80,4.34]		4.14[3.90,4.42]	4.00[3.80,4.20]	
Chloride(mmol/L)	Mexican American	104.00[102.00,106.00]	104.00[102.00,106.00]	102.00[100.00,104.00]	<0.001	103.00[100.74,105.00]	103.00[102.00,105.00]	0.006
	Other Hispanic	103.00[101.92,105.00]	103.44[101.00,105.00]	101.00[99.00,103.95]		103.00[100.59,105.00]	103.00[101.60,105.00]	
	Non-Hispanic White	103.50[102.00,105.00]	103.00[101.00,105.00]	102.00[100.00,104.00]		102.60[100.00,105.00]	103.00[101.00,105.00]	
	Non-Hispanic Black	104.00[102.00,106.00]	104.00[102.00,105.00]	103.00[100.00,105.00]		103.00[101.00,105.00]	104.00[102.00,105.00]	
	Other Race - Including Multi-Racial	103.00[102.00,105.00]	103.00[101.00,105.00]	102.00[100.00,104.00]		102.95[101.00,105.00]	103.31[101.00,105.00]	
Transferrin Saturation (%)	Mexican American	24.10[17.00,33.47]	23.00[16.90,31.00]	23.00[15.00,30.00]	<0.001	23.70[17.70,30.45]	24.80[19.17,33.06]	<0.001
	Other Hispanic	23.91[17.34,32.00]	23.55[18.74,31.11]	22.00[16.90,28.51]		23.75[19.66,31.00]	20.97[15.88,29.19]	
	Non-Hispanic White	25.00[18.40,33.00]	23.50[17.80,30.00]	24.00[17.63,29.00]		23.15[15.27,29.29]	24.30[18.50,30.70]	
	Non-Hispanic Black	21.80[15.30,30.00]	21.85[16.00,28.00]	20.60[15.60,27.00]		19.89[15.11,26.20]	21.10[17.00,28.56]	
	Other Race - Including Multi-Racial	25.00[17.90,32.89]	24.07[18.07,30.54]	23.00[16.58,31.00]		21.47[16.79,33.34]	22.68[17.42,29.66]	
Globulin (g/L)	Mexican American	30.00[27.00,32.00]	31.00[28.00,34.00]	31.00[28.00,34.00]	<0.001	31.00[28.00,34.00]	29.00[26.00,32.00]	<0.001
	Other Hispanic	30.00[27.00,32.00]	31.00[28.00,33.63]	31.00[29.00,34.00]		31.00[28.00,34.00]	30.00[28.00,33.00]	
	Non-Hispanic White	28.00[25.00,30.00]	28.00[26.00,31.00]	29.00[26.00,31.00]		30.00[27.00,33.68]	28.00[25.00,31.00]	
	Non-Hispanic Black	31.00[28.00,34.00]	32.00[29.00,35.00]	33.00[30.00,36.00]		33.00[30.00,36.00]	32.00[29.00,35.00]	
	Other Race - Including Multi-Racial	29.00[27.00,32.00]	30.00[27.00,32.36]	30.00[28.00,33.00]		31.00[29.48,36.00]	29.00[26.00,32.00]	
alpha-carotene(umol/L)	Mexican American	0.06[0.03,0.10]	0.06[0.04,0.10]	0.06[0.04,0.10]	<0.001	0.06[0.03,0.10]	0.05[0.04,0.10]	0.002
	Other Hispanic	0.07[0.04,0.13]	0.09[0.04,0.16]	0.05[0.03,0.11]		0.06[0.04,0.11]	0.07[0.03,0.12]	
	Non-Hispanic White	0.05[0.03,0.10]	0.05[0.03,0.09]	0.04[0.02,0.07]		0.05[0.02,0.09]	0.06[0.04,0.12]	

	Non-Hispanic Black	0.03[0.02,0.07]	0.04[0.02,0.08]	0.03[0.02,0.07]		0.03[0.02,0.05]	0.05[0.02,0.09]	
	Other Race - Including Multi-Racial	0.06[0.03,0.12]	0.08[0.04,0.12]	0.06[0.03,0.10]		0.06[0.05,0.12]	0.10[0.05,0.12]	
trans-beta-carotene(umol/L)	Mexican American	0.23[0.14,0.40]	0.24[0.13,0.38]	0.20[0.12,0.35]	<0.001	0.32[0.18,0.53]	0.30[0.15,0.43]	0.085
	Other Hispanic	0.24[0.13,0.42]	0.25[0.14,0.44]	0.17[0.10,0.36]		0.34[0.18,0.45]	0.35[0.23,0.40]	
	Non-Hispanic White	0.23[0.13,0.42]	0.22[0.13,0.39]	0.17[0.09,0.32]		0.30[0.16,0.54]	0.34[0.20,0.56]	
	Non-Hispanic Black	0.19[0.11,0.34]	0.21[0.12,0.38]	0.20[0.10,0.34]		0.37[0.15,0.49]	0.32[0.20,0.53]	
	Other Race - Including Multi-Racial	0.24[0.13,0.46]	0.32[0.17,0.52]	0.20[0.10,0.49]		0.20[0.18,0.49]	0.40[0.25,0.65]	
cis-beta-carotene(umol/L)	Mexican American	0.01[0.01,0.02]	0.01[0.01,0.02]	0.01[0.01,0.02]	<0.001	0.02[0.01,0.03]	0.01[0.01,0.02]	0.012
	Other Hispanic	0.01[0.01,0.02]	0.01[0.01,0.02]	0.01[0.01,0.02]		0.02[0.01,0.02]	0.02[0.02,0.02]	
	Non-Hispanic White	0.01[0.01,0.03]	0.01[0.01,0.02]	0.01[0.01,0.02]		0.02[0.01,0.03]	0.02[0.01,0.03]	
	Non-Hispanic Black	0.01[0.01,0.02]	0.01[0.01,0.02]	0.01[0.01,0.02]		0.02[0.01,0.03]	0.02[0.01,0.03]	
	Other Race - Including Multi-Racial	0.01[0.01,0.03]	0.02[0.01,0.03]	0.01[0.01,0.03]		0.02[0.01,0.03]	0.02[0.02,0.03]	
beta-cryptoxanthin(umol/L)	Mexican American	0.23[0.14,0.36]	0.22[0.14,0.36]	0.20[0.12,0.33]	<0.001	0.22[0.09,0.39]	0.19[0.13,0.31]	<0.001
	Other Hispanic	0.15[0.09,0.23]	0.14[0.09,0.26]	0.14[0.09,0.25]		0.13[0.07,0.17]	0.24[0.12,0.29]	
	Non-Hispanic White	0.12[0.08,0.19]	0.10[0.07,0.16]	0.09[0.05,0.13]		0.13[0.07,0.20]	0.14[0.09,0.22]	
	Non-Hispanic Black	0.13[0.09,0.20]	0.13[0.09,0.22]	0.11[0.07,0.17]		0.10[0.07,0.19]	0.17[0.11,0.28]	
	Other Race - Including Multi-Racial	0.15[0.09,0.25]	0.16[0.09,0.25]	0.13[0.08,0.24]		0.25[0.09,0.27]	0.18[0.14,0.31]	
Lutein and zeaxanthin(umol/L)	Mexican American	0.28[0.21,0.38]	0.32[0.21,0.44]	0.31[0.22,0.44]	<0.001	0.27[0.18,0.39]	0.28[0.21,0.42]	0.039
	Other Hispanic	0.28[0.20,0.38]	0.27[0.20,0.40]	0.33[0.20,0.49]		0.25[0.19,0.36]	0.26[0.17,0.47]	
	Non-Hispanic White	0.24[0.17,0.34]	0.25[0.18,0.36]	0.23[0.16,0.32]		0.23[0.18,0.37]	0.27[0.19,0.38]	
	Non-Hispanic Black	0.26[0.20,0.37]	0.29[0.21,0.40]	0.29[0.20,0.38]		0.31[0.21,0.40]	0.33[0.25,0.45]	
	Other Race - Including Multi-Racial	0.31[0.21,0.44]	0.33[0.25,0.49]	0.35[0.21,0.52]		0.18[0.13,0.35]	0.34[0.26,0.58]	
trans-lycopene(umol/L)	Mexican American	0.38[0.28,0.51]	0.35[0.26,0.50]	0.33[0.25,0.44]	<0.001	0.28[0.15,0.36]	0.31[0.20,0.44]	0.006
	Other Hispanic	0.41[0.29,0.54]	0.34[0.22,0.50]	0.40[0.27,0.57]		0.26[0.21,0.39]	0.31[0.19,0.51]	
	Non-Hispanic White	0.42[0.30,0.56]	0.37[0.26,0.54]	0.34[0.21,0.49]		0.33[0.21,0.43]	0.34[0.22,0.50]	

	Non-Hispanic Black	0.43[0.29,0.58]	0.41[0.28,0.56]	0.34[0.23,0.51]		0.25[0.15,0.37]	0.29[0.20,0.42]	
	Other Race - Including Multi-Racial	0.37[0.23,0.51]	0.36[0.22,0.56]	0.33[0.20,0.50]		0.14[0.13,0.26]	0.28[0.16,0.46]	
VitaminD(nmol/L)	Mexican American	53.20[40.90,65.80]	51.60[39.80,63.70]	46.80[35.00,56.80]	<0.001	53.90[39.92,72.00]	51.60[39.70,61.10]	<0.001
	Other Hispanic	55.83[44.70,68.20]	44.13[37.43,58.70]	53.20[42.17,58.70]		45.71[38.11,66.82]	56.30[37.30,65.64]	
	Non-Hispanic White	66.50[54.40,80.30]	59.20[48.30,72.90]	58.70[45.90,72.90]		58.70[44.40,70.60]	63.50[51.60,75.40]	
	Non-Hispanic Black	37.50[27.90,50.80]	37.50[28.80,50.80]	38.09[30.20,51.23]		40.35[30.20,58.70]	45.26[32.69,58.70]	
	Other Race - Including Multi-Racial	50.80[39.80,64.10]	49.20[35.00,63.67]	53.20[36.95,66.35]		61.21[48.14,69.49]	55.39[39.93,64.92]	
Creatine Phosphokinase (CPK) (IU/L)	Mexican American	109.00[76.00,163.00]	127.63[87.00,187.00]	96.00[66.00,136.64]	<0.001	102.27[60.54,159.00]	102.60[73.00,140.92]	<0.001
	Other Hispanic	110.00[76.00,177.87]	121.00[86.00,184.89]	100.57[70.00,146.33]		103.00[74.00,160.00]	96.00[68.00,136.13]	
	Non-Hispanic White	100.00[70.00,149.00]	99.00[71.00,149.00]	89.00[61.00,136.00]		74.00[55.00,107.60]	94.00[65.00,128.00]	
	Non-Hispanic Black	160.00[105.00,251.31]	182.00[119.96,300.99]	157.69[98.00,265.00]		168.01[98.41,250.07]	153.00[93.88,236.00]	
	Other Race - Including Multi-Racial	102.00[72.00,156.00]	121.29[82.00,187.99]	101.07[74.00,160.00]		94.32[82.77,149.95]	103.16[76.00,151.00]	
Direct HDL-Cholesterol(mmol/L)	Mexican American	1.27[1.06,1.53]	1.16[0.98,1.40]	1.14[0.98,1.34]	<0.001	1.22[1.03,1.40]	1.28[1.09,1.55]	<0.001
	Other Hispanic	1.29[1.09,1.58]	1.16[1.01,1.42]	1.16[0.98,1.42]		1.27[1.06,1.45]	1.27[1.09,1.45]	
	Non-Hispanic White	1.37[1.11,1.68]	1.27[1.06,1.55]	1.14[0.96,1.37]		1.28[1.07,1.65]	1.37[1.14,1.71]	
	Non-Hispanic Black	1.42[1.19,1.73]	1.34[1.11,1.63]	1.27[1.06,1.55]		1.32[1.09,1.64]	1.42[1.19,1.71]	
	Other Race - Including Multi-Racial	1.34[1.11,1.63]	1.27[1.06,1.55]	1.16[0.96,1.42]		1.37[1.10,1.60]	1.34[1.03,1.66]	
Direct HDL-Cholesterol (mg/dL)	Mexican American	48.00[41.00,59.00]	45.00[38.00,54.00]	44.00[38.00,52.00]	<0.001	46.00[39.00,56.00]	49.00[42.00,60.00]	<0.001
	Other Hispanic	49.00[41.00,60.00]	45.00[38.00,55.00]	44.00[37.37,53.00]		47.00[40.00,56.00]	48.00[41.00,56.96]	
	Non-Hispanic White	52.00[43.00,64.00]	49.00[41.00,59.00]	43.00[36.00,52.00]		48.00[40.00,61.00]	52.00[43.00,65.00]	
	Non-Hispanic Black	55.00[45.00,66.00]	51.00[43.00,63.00]	49.00[41.00,59.00]		52.00[43.00,66.00]	55.00[45.00,65.27]	
	Other Race - Including Multi-Racial	52.00[43.00,62.00]	48.00[41.00,59.00]	45.00[37.00,55.00]		53.00[40.48,61.75]	52.00[41.00,64.49]	
Total Cholesterol(mmol/L)	Mexican American	4.84[4.22,5.51]	5.22[4.53,5.95]	4.94[4.24,5.82]	<0.001	5.02[4.48,5.72]	5.20[4.42,5.82]	0.123
	Other Hispanic	4.84[4.19,5.53]	5.30[4.65,5.99]	5.09[4.32,5.87]		5.29[4.54,6.12]	5.29[4.68,5.92]	
	Non-Hispanic White	5.02[4.37,5.74]	5.21[4.55,5.95]	4.63[3.96,5.51]		5.10[4.27,6.00]	5.20[4.53,5.90]	

	Non-Hispanic Black	4.68[4.09,5.40]	5.04[4.37,5.74]	4.84[4.11,5.64]		5.09[4.36,5.90]	5.07[4.34,5.82]	
	Other Race - Including Multi-Racial	4.81[4.22,5.48]	5.30[4.57,6.00]	4.83[4.02,5.56]		4.90[4.30,5.84]	4.99[4.27,5.80]	
Cholesterol, total (mmol/L)	Mexican American	4.84[4.24,5.53]	5.22[4.53,5.92]	4.96[4.22,5.82]		4.99[4.45,5.78]	5.17[4.37,5.84]	
	Other Hispanic	4.84[4.19,5.53]	5.26[4.63,6.00]	5.04[4.27,5.85]		5.25[4.42,6.00]	5.25[4.63,5.92]	
	Non-Hispanic White	5.02[4.37,5.74]	5.22[4.52,5.95]	4.63[3.93,5.48]	<0.001	5.04[4.24,5.90]	5.15[4.45,5.82]	0.095
	Non-Hispanic Black	4.66[4.06,5.35]	4.99[4.32,5.69]	4.78[4.05,5.59]		5.05[4.24,5.77]	4.97[4.28,5.74]	
	Other Race - Including Multi-Racial	4.81[4.24,5.53]	5.31[4.55,5.97]	4.86[4.03,5.64]		5.02[4.29,6.05]	4.94[4.19,5.84]	
Triglyceride (mg/dL)	Mexican American	105.00[74.00,152.00]	128.00[89.00,187.61]	154.65[111.00,231.66]		134.00[107.00,178.95]	124.94[92.95,178.00]	
	Other Hispanic	98.00[68.00,142.00]	127.00[92.00,177.00]	142.32[105.00,212.48]		139.04[95.00,178.11]	131.06[98.00,170.26]	
	Non-Hispanic White	100.00[69.00,146.00]	125.00[90.00,180.00]	152.00[102.47,211.00]	<0.001	118.35[80.00,180.44]	122.00[83.00,172.02]	<0.001
	Non-Hispanic Black	74.00[55.00,104.00]	84.00[61.00,118.00]	99.00[73.00,140.64]		87.51[70.20,122.00]	90.04[66.07,124.00]	
	Other Race - Including Multi-Racial	94.81[65.00,140.00]	112.00[84.12,162.60]	144.00[92.00,197.15]		134.13[106.54,160.29]	126.69[86.04,183.28]	
Triglyceride (mmol/L)	Mexican American	1.19[0.84,1.72]	1.45[1.00,2.12]	1.75[1.25,2.61]		1.51[1.20,2.02]	1.41[1.05,2.01]	
	Other Hispanic	1.11[0.77,1.60]	1.43[1.04,2.00]	1.61[1.19,2.40]		1.57[1.07,2.01]	1.48[1.11,1.92]	
	Non-Hispanic White	1.13[0.78,1.65]	1.41[1.02,2.03]	1.72[1.16,2.38]	<0.001	1.33[0.90,2.03]	1.38[0.94,1.94]	<0.001
	Non-Hispanic Black	0.84[0.62,1.17]	0.95[0.69,1.33]	1.12[0.82,1.59]		0.99[0.79,1.38]	1.02[0.75,1.40]	
	Other Race - Including Multi-Racial	1.07[0.73,1.58]	1.26[0.95,1.84]	1.63[1.04,2.23]		1.52[1.20,1.81]	1.43[0.97,2.07]	
LDL-cholesterol(mmol/L)	Mexican American	2.87[2.33,3.44]	3.10[2.51,3.69]	2.89[2.17,3.54]		2.97[2.56,3.54]	2.89[2.35,3.41]	
	Other Hispanic	2.92[2.35,3.49]	3.23[2.66,3.80]	2.74[2.28,3.47]		3.37[2.52,3.71]	3.22[2.57,3.72]	
	Non-Hispanic White	2.92[2.38,3.54]	3.08[2.48,3.70]	2.48[1.94,3.18]	<0.001	2.71[2.20,3.47]	3.00[2.43,3.59]	<0.001
	Non-Hispanic Black	2.74[2.17,3.36]	3.05[2.48,3.70]	2.77[2.17,3.50]		2.92[2.26,3.77]	3.03[2.46,3.64]	
	Other Race - Including Multi-Racial	2.82[2.29,3.36]	3.13[2.48,3.85]	2.50[1.87,3.25]		3.03[1.74,3.59]	2.56[1.89,3.32]	
Glycohemoglobin(%)	Mexican American	5.26[5.10,5.40]	5.80[5.70,6.00]	7.50[6.70,9.20]		6.00[5.60,6.90]	5.70[5.40,6.30]	
	Other Hispanic	5.20[5.00,5.40]	5.80[5.70,6.00]	7.30[6.50,9.23]	<0.001	5.86[5.50,6.34]	5.70[5.40,6.00]	<0.001
	Non-Hispanic White	5.20[5.00,5.40]	5.80[5.70,6.00]	6.80[6.30,7.74]		5.60[5.30,6.00]	5.60[5.30,5.90]	

	Non-Hispanic Black	5.30[5.10,5.50]	5.90[5.70,6.00]	7.00[6.50,8.40]		6.00[5.50,6.70]	5.90[5.50,6.30]	
	Other Race - Including Multi-Racial	5.30[5.10,5.40]	5.80[5.70,6.00]	7.00[6.50,8.20]		6.14[5.50,6.80]	5.90[5.50,6.20]	
Glucose, serum (mmol/L)	Mexican American	4.94[4.61,5.27]	5.44[5.00,5.88]	8.33[6.38,12.10]	<0.001	5.77[5.16,7.11]	5.38[5.00,6.42]	<0.001
	Other Hispanic	4.88[4.61,5.27]	5.38[4.94,5.94]	7.84[6.16,11.77]		5.44[5.11,6.14]	5.27[4.88,5.92]	
	Non-Hispanic White	4.94[4.61,5.27]	5.38[5.00,5.94]	7.27[5.88,9.71]		5.55[5.05,6.41]	5.33[4.94,5.94]	
	Non-Hispanic Black	4.83[4.50,5.16]	5.16[4.83,5.65]	7.16[5.72,9.83]		5.54[5.05,6.92]	5.40[4.94,6.16]	
	Other Race - Including Multi-Racial	4.94[4.61,5.27]	5.38[5.00,5.83]	7.33[5.72,9.60]		5.72[5.03,6.72]	5.50[5.05,6.38]	
Glucose, plasma (mg/dL)	Mexican American	96.20[91.00,102.00]	105.48[99.00,114.00]	155.00[127.80,215.00]	<0.001	110.96[99.65,131.96]	105.00[97.98,121.00]	0.017
	Other Hispanic	95.00[89.70,101.00]	107.00[99.00,114.00]	156.75[126.08,214.74]		107.00[99.00,120.02]	104.23[94.56,114.00]	
	Non-Hispanic White	96.00[90.00,102.00]	106.00[99.00,114.00]	141.00[121.00,178.00]		107.29[95.62,129.58]	103.00[95.30,113.00]	
	Non-Hispanic Black	92.60[87.30,98.00]	100.37[94.00,108.00]	139.26[112.42,179.00]		102.16[93.10,118.77]	104.18[96.00,116.59]	
	Other Race - Including Multi-Racial	96.00[90.00,101.78]	105.00[97.98,111.64]	131.33[113.11,161.00]		103.93[95.20,120.10]	106.13[97.00,116.00]	
Plasma glucose: SI(mmol/L)	Mexican American	5.34[5.05,5.66]	5.86[5.50,6.33]	8.60[7.09,11.94]	<0.001	6.16[5.54,7.33]	5.83[5.44,6.71]	0.016
	Other Hispanic	5.27[4.98,5.61]	5.94[5.50,6.33]	8.70[7.00,11.92]		5.94[5.50,6.67]	5.79[5.25,6.33]	
	Non-Hispanic White	5.33[5.00,5.66]	5.88[5.50,6.33]	7.83[6.72,9.88]		5.96[5.31,7.20]	5.72[5.29,6.27]	
	Non-Hispanic Black	5.14[4.85,5.44]	5.58[5.22,6.00]	7.74[6.25,9.94]		5.67[5.17,6.59]	5.78[5.33,6.47]	
	Other Race - Including Multi-Racial	5.33[5.00,5.65]	5.83[5.44,6.20]	7.30[6.28,8.94]		5.77[5.29,6.67]	5.89[5.38,6.44]	
C-peptide:SI(nmol/L)	Mexican American	0.72[0.55,0.94]	0.94[0.73,1.32]	1.01[0.72,1.28]	<0.001	0.89[0.70,1.16]	0.89[0.70,1.16]	0.002
	Other Hispanic	0.68[0.51,0.92]	0.99[0.76,1.16]	0.92[0.68,1.16]		0.90[0.70,1.14]	0.82[0.65,1.11]	
	Non-Hispanic White	0.66[0.50,0.90]	1.02[0.77,1.33]	1.13[0.85,1.62]		0.98[0.61,1.40]	0.82[0.60,1.10]	
	Non-Hispanic Black	0.60[0.46,0.80]	0.84[0.60,1.14]	0.99[0.76,1.27]		0.90[0.66,1.13]	0.79[0.57,0.97]	
	Other Race - Including Multi-Racial	0.62[0.48,0.82]	0.75[0.58,1.13]	0.69[0.50,1.09]		0.79[0.39,0.97]	0.66[0.60,0.79]	
Insulin(uU/mL)	Mexican American	10.23[6.79,15.55]	14.28[9.24,22.08]	14.42[8.95,23.90]	<0.001	12.04[8.88,18.45]	11.38[6.98,17.90]	0.04
	Other Hispanic	9.27[6.15,13.77]	12.62[8.60,20.00]	13.99[8.19,23.40]		11.67[8.14,16.16]	11.27[8.30,15.59]	
	Non-Hispanic White	7.94[5.29,12.30]	11.42[7.02,18.13]	14.41[8.97,24.77]		11.15[6.70,16.85]	9.89[6.44,15.07]	

	Non-Hispanic Black	8.77[5.94,13.67]	11.44[7.28,18.70]	13.83[8.20,22.27]		10.45[6.62,15.09]	11.97[7.10,16.93]	
	Other Race - Including Multi-Racial	8.22[5.12,11.86]	11.31[7.02,17.87]	10.91[6.98,18.24]		9.58[6.55,15.91]	8.89[5.47,12.96]	
Insulin:SI(pmol/L)	Mexican American	63.06[45.32,91.57]	94.81[66.45,131.29]	96.57[58.60,129.65]		73.72[50.81,107.93]	79.01[53.75,108.53]	
	Other Hispanic	64.71[46.07,84.43]	82.66[56.50,115.07]	103.48[78.71,148.68]		72.11[57.36,88.58]	65.19[48.77,71.68]	
	Non-Hispanic White	50.70[37.54,72.30]	82.73[54.18,112.91]	120.54[65.45,181.73]	<0.001	69.90[42.79,126.99]	58.52[42.30,88.48]	0.014
	Non-Hispanic Black	55.26[38.63,80.82]	82.18[53.60,124.86]	116.49[80.41,145.16]		72.32[44.31,105.17]	77.47[50.17,100.93]	
	Other Race - Including Multi-Racial	59.86[40.57,82.05]	71.27[42.67,123.86]	55.06[43.79,77.09]		53.51[31.56,77.14]	58.99[40.07,86.88]	
Two Hour Glucose(OGTT)(mg/dL)	Mexican American	101.00[84.00,123.00]	126.00[102.00,158.80]	299.71[259.73,421.07]		156.74[128.39,199.75]	140.32[108.00,160.71]	
	Other Hispanic	97.00[81.84,119.84]	125.00[100.08,155.00]	305.78[225.72,376.44]		139.00[121.19,210.39]	122.39[107.12,159.53]	
	Non-Hispanic White	100.00[82.00,122.00]	130.00[102.00,166.00]	272.46[196.92,313.37]	<0.001	160.17[112.25,196.90]	118.00[95.00,155.13]	0.002
	Non-Hispanic Black	95.00[81.00,114.00]	113.73[93.00,138.32]	218.97[156.57,280.76]		126.55[102.84,150.34]	123.35[102.00,154.00]	
	Other Race - Including Multi-Racial	100.00[85.00,122.64]	125.15[98.00,155.00]	283.29[227.09,363.80]		117.65[114.05,145.35]	124.00[102.00,152.67]	

Supplementary Table 8. Survival status subgroup comparison of laboratory characteristics between different disease groups

Terms	Survival status	Normal	Prediabetes	T2D	p	Normal	MCI	p
White blood cell count(1000 cells/uL)	Assumed alive	6.90[5.70,8.20]	7.10[5.90,8.60]	7.60[6.30,9.00]	<0.001	6.80[5.60,7.80]	6.60[5.60,7.90]	<0.001
	Assumed deceased	6.80[5.60,8.10]	7.40[6.10,8.80]	7.60[6.30,9.17]		7.10[5.90,8.40]	7.10[5.90,8.20]	
Lymphocyte percent(%)	Assumed alive	30.00[25.00,35.20]	30.60[25.50,35.80]	28.90[23.60,34.40]	<0.001	29.00[23.40,35.21]	28.70[23.80,33.80]	<0.001
	Assumed deceased	27.00[21.50,33.10]	27.30[21.30,33.00]	26.10[21.10,32.00]		25.90[20.40,31.70]	26.10[20.90,32.10]	
Segmented neutrophils percent(%)	Assumed alive	58.60[52.60,64.20]	57.80[51.80,63.60]	59.80[53.50,65.60]	<0.001	59.30[51.30,65.60]	59.30[53.40,64.80]	<0.001
	Assumed deceased	60.90[54.00,66.90]	60.70[54.10,66.90]	61.80[54.93,67.30]		61.40[54.90,67.20]	61.60[54.90,66.90]	
Eosinophils percent(%)	Assumed alive	2.30[1.50,3.40]	2.50[1.60,3.70]	2.40[1.70,3.60]	<0.001	2.60[1.60,3.70]	2.60[1.70,3.80]	0.816
	Assumed deceased	2.30[1.50,3.60]	2.60[1.70,3.80]	2.50[1.70,3.80]		2.50[1.70,3.70]	2.50[1.70,3.60]	
Basophils percent(%)	Assumed alive	0.60[0.40,0.90]	0.70[0.50,0.90]	0.70[0.50,0.90]	<0.001	0.60[0.40,0.90]	0.70[0.50,0.90]	<0.001
	Assumed deceased	0.60[0.40,0.90]	0.60[0.40,0.90]	0.60[0.40,0.90]		0.60[0.40,0.80]	0.60[0.40,0.90]	
Lymphocyte number(1000 cells/uL)	Assumed alive	2.00[1.60,2.50]	2.20[1.70,2.70]	2.10[1.70,2.70]	<0.001	1.90[1.60,2.50]	1.80[1.50,2.30]	0.001
	Assumed deceased	1.80[1.40,2.30]	1.90[1.50,2.40]	2.00[1.50,2.50]		1.80[1.30,2.30]	1.80[1.40,2.20]	
Monocyte number(1000cells/uL)	Assumed alive	0.50[0.40,0.60]	0.60[0.40,0.70]	0.60[0.40,0.70]	<0.001	0.50[0.40,0.60]	0.50[0.40,0.70]	<0.001
	Assumed deceased	0.60[0.50,0.70]	0.60[0.50,0.80]	0.60[0.50,0.70]		0.60[0.50,0.70]	0.60[0.50,0.70]	
Segmented neutrophils num(1000 cells/uL)	Assumed alive	4.00[3.10,5.10]	4.10[3.20,5.20]	4.50[3.50,5.60]	<0.001	3.90[3.00,4.90]	3.80[3.10,4.80]	<0.001
	Assumed deceased	4.10[3.20,5.10]	4.40[3.50,5.60]	4.60[3.60,5.80]		4.30[3.50,5.30]	4.20[3.40,5.20]	
Eosinophils number(1000 cells/uL)	Assumed alive	0.20[0.10,0.20]	0.20[0.10,0.30]	0.20[0.10,0.30]	<0.001	0.20[0.10,0.20]	0.20[0.10,0.30]	0.83
	Assumed deceased	0.20[0.10,0.20]	0.20[0.10,0.30]	0.20[0.10,0.30]		0.20[0.10,0.30]	0.20[0.10,0.30]	
Basophils number(1000 cells/uL)	Assumed alive	0.00[0.00,0.10]	0.00[0.00,0.10]	0.10[0.00,0.10]	<0.001	0.00[0.00,0.10]	0.00[0.00,0.10]	0.001
	Assumed deceased	0.00[0.00,0.10]	0.00[0.00,0.10]	0.00[0.00,0.10]		0.00[0.00,0.10]	0.00[0.00,0.10]	
Red blood cell count(millioncells/uL)	Assumed alive	4.71[4.39,5.06]	4.72[4.42,5.05]	4.74[4.39,5.06]	<0.001	4.51[4.18,4.82]	4.56[4.29,4.85]	0.175
	Assumed deceased	4.58[4.22,4.93]	4.62[4.28,4.96]	4.58[4.18,4.95]		4.53[4.12,4.88]	4.55[4.24,4.84]	
Hemoglobin (g/dL)	Assumed alive	14.40[13.50,15.40]	14.20[13.30,15.10]	14.20[13.10,15.10]	<0.001	13.70[12.50,14.60]	14.10[13.30,15.00]	<0.001

	Assumed deceased	14.30[13.30,15.40]	14.20[13.20,15.20]	14.00[12.70,15.00]		14.00[12.70,15.10]	14.10[13.30,15.00]	
Hematocrit (%)	Assumed alive	42.40[39.30,45.30]	42.00[39.08,44.90]	41.70[38.50,44.40]	<0.001	40.60[37.61,43.40]	41.47[39.00,44.20]	0.001
	Assumed deceased	42.30[39.30,45.30]	42.10[39.20,45.20]	41.42[38.00,44.49]		41.60[37.90,44.93]	41.90[39.20,44.50]	
Mean cell volume(fL)	Assumed alive	90.10[87.20,92.80]	89.30[85.80,92.20]	88.80[85.50,91.65]	<0.001	90.50[86.80,93.40]	91.50[88.70,94.20]	<0.001
	Assumed deceased	92.60[89.40,95.90]	91.40[88.36,94.30]	90.40[86.90,94.02]		92.30[88.60,95.60]	92.03[89.40,95.20]	
Mean cell hemoglobin(pg)	Assumed alive	30.70[29.60,31.80]	30.20[28.80,31.40]	30.10[28.80,31.30]	<0.001	30.60[29.00,31.70]	31.20[30.00,32.20]	<0.001
	Assumed deceased	31.50[30.20,32.70]	30.90[29.80,32.10]	30.70[29.20,32.10]		31.00[29.60,32.50]	31.30[30.20,32.50]	
Mean Cell Hgb Conc.(g/dL)	Assumed alive	34.00[33.50,34.60]	33.80[33.20,34.30]	33.80[33.20,34.40]	<0.001	33.70[33.10,34.30]	34.00[33.40,34.70]	<0.001
	Assumed deceased	34.00[33.40,34.50]	33.80[33.30,34.30]	33.80[33.20,34.40]		33.70[33.10,34.30]	33.90[33.40,34.40]	
Red cell distribution width(%)	Assumed alive	12.60[12.20,13.20]	13.20[12.60,13.90]	13.20[12.50,13.90]	<0.001	13.30[12.70,14.10]	13.00[12.50,13.70]	<0.001
	Assumed deceased	12.80[12.30,13.50]	13.10[12.50,13.90]	13.10[12.50,14.10]		13.10[12.50,13.90]	12.90[12.40,13.50]	
Platelet count(1000cells/uL)	Assumed alive	247.00[212.00,289.00]	250.00[211.00,295.00]	240.00[201.00,293.00]	<0.001	223.52[189.00,272.56]	229.00[195.00,269.00]	0.035
	Assumed deceased	242.00[200.00,290.32]	246.00[203.00,296.00]	235.00[193.00,282.66]		233.00[189.00,278.00]	239.00[197.00,282.00]	
Mean platelet volume(fL)	Assumed alive	8.10[7.60,8.70]	8.10[7.60,8.80]	8.20[7.60,8.90]	<0.001	8.40[7.70,9.10]	8.20[7.70,8.90]	0.009
	Assumed deceased	8.00[7.50,8.60]	8.00[7.50,8.60]	8.20[7.60,8.80]		8.30[7.70,8.90]	8.10[7.60,8.80]	
Folate, RBC (nmol/L RBC)	Assumed alive	831.30[591.20,1164.20]	963.00[681.00,1350.00]	1080.00[765.90,1480.00]	<0.001	926.13[672.33,1340.75]	1150.00[832.00,1600.00]	<0.001
	Assumed deceased	806.30[573.00,1130.00]	890.08[628.00,1340.00]	912.80[652.30,1420.00]		812.88[566.99,1204.79]	890.10[654.60,1240.00]	
Folate, serum(nmol/L)	Assumed alive	29.20[20.60,41.40]	31.70[21.50,47.63]	33.50[23.54,50.03]	<0.001	31.55[21.50,41.00]	40.79[27.90,55.65]	0.052
	Assumed deceased	35.07[22.70,54.40]	36.70[23.42,57.36]	34.31[23.60,54.80]		34.00[23.10,49.60]	39.90[26.84,58.90]	
Vitamin B12(pmol/L)	Assumed alive	346.12[264.90,458.30]	365.83[273.10,487.08]	367.50[271.58,519.60]	<0.001	354.22[257.16,510.70]	386.70[281.87,547.48]	0.007
	Assumed deceased	354.32[256.82,483.39]	350.55[250.19,484.87]	351.30[261.25,505.91]		363.71[256.64,526.37]	362.63[263.46,487.10]	
Homocysteine(umol/L)	Assumed alive	7.51[6.26,9.00]	8.04[6.74,9.58]	7.89[6.29,9.58]	<0.001	8.37[6.97,10.83]	8.43[7.12,10.05]	<0.001
	Assumed deceased	9.54[7.66,12.13]	9.97[8.13,12.06]	10.01[8.03,12.46]		10.77[8.49,13.51]	9.60[7.92,11.71]	
Blood mercury, total(nmol/L)	Assumed alive	4.49[2.30,8.98]	4.60[2.40,9.20]	4.05[2.20,8.25]	0.001	4.27[1.80,8.58]	5.30[2.80,10.95]	0.012
	Assumed deceased	4.29[2.20,8.48]	4.50[2.20,8.50]	3.60[2.00,7.20]		3.10[1.70,5.50]	3.60[2.00,7.69]	

Mercury, inorganic(nmol/L)	Assumed alive	1.25[1.25,1.50]	1.25[0.95,1.50]	1.25[0.95,1.50]	<0.001	0.95[0.95,1.45]	0.95[0.95,1.80]	0.014
	Assumed deceased	1.40[1.25,1.50]	1.25[1.25,1.50]	1.25[1.25,1.50]		0.95[0.95,0.95]	0.95[0.95,1.40]	
Tot Iron Binding Capacity TIBC(umol/L)	Assumed alive	62.47[56.21,69.99]	60.68[54.98,67.13]	60.71[54.80,66.95]	<0.001	60.78[55.10,67.25]	64.08[58.00,70.51]	0.182
	Assumed deceased	63.19[56.21,70.71]	63.55[56.03,71.60]	64.19[56.39,71.07]		63.19[56.21,70.53]	63.70[56.39,70.53]	
Ferritin(ug/L)	Assumed alive	63.00[29.00,125.00]	86.96[41.38,163.32]	103.00[47.33,205.00]	<0.001	126.36[59.00,183.67]	100.99[56.68,182.00]	0.839
	Assumed deceased	98.00[50.00,179.44]	117.00[56.00,195.00]	126.02[66.00,236.00]		110.00[56.93,200.17]	107.00[54.87,187.97]	
Cotinine, Serum (ng/mL)	Assumed alive	0.05[0.01,18.30]	0.04[0.01,23.00]	0.04[0.01,0.57]	<0.001	0.04[0.01,0.27]	0.02[0.01,0.08]	<0.001
	Assumed deceased	0.08[0.02,149.00]	0.06[0.02,64.08]	0.06[0.02,3.93]		0.06[0.03,1.00]	0.04[0.02,0.20]	
gamma-tocopherol (umol/L)	Assumed alive	4.64[3.10,6.41]	5.03[3.36,7.28]	5.33[3.41,7.85]	<0.001	4.46[2.90,7.72]	3.93[2.19,6.65]	0.003
	Assumed deceased	4.59[2.56,6.91]	5.09[3.05,7.71]	5.96[3.79,8.55]		4.71[2.79,7.64]	4.64[2.40,7.35]	
Retinyl palmitate (umol/L)	Assumed alive	0.05[0.03,0.09]	0.05[0.03,0.08]	0.05[0.03,0.09]	<0.001	0.05[0.03,0.08]	0.07[0.04,0.12]	<0.001
	Assumed deceased	0.06[0.03,0.09]	0.06[0.03,0.09]	0.06[0.03,0.12]		0.05[0.03,0.09]	0.06[0.04,0.10]	
Retinyl stearate (umol/L)	Assumed alive	0.02[0.01,0.02]	0.02[0.01,0.02]	0.02[0.02,0.02]	<0.001	0.01[0.01,0.02]	0.01[0.01,0.02]	0.785
	Assumed deceased	0.01[0.01,0.02]	0.01[0.01,0.02]	0.02[0.01,0.03]		0.01[0.01,0.01]	0.01[0.01,0.01]	
Retinol (umol/L)	Assumed alive	1.95[1.62,2.35]	1.94[1.62,2.33]	2.01[1.65,2.42]	<0.001	2.04[1.63,2.55]	2.30[2.01,2.65]	<0.001
	Assumed deceased	2.17[1.79,2.59]	2.17[1.80,2.63]	2.24[1.80,2.67]		2.14[1.77,2.58]	2.26[1.91,2.69]	
Albumin, urine(ug/mL)	Assumed alive	6.60[3.40,12.20]	7.41[4.00,14.80]	11.60[5.40,29.30]	<0.001	12.74[5.71,29.90]	7.00[3.60,14.40]	<0.001
	Assumed deceased	8.80[4.30,20.00]	10.60[4.90,26.91]	20.80[7.70,84.43]		17.86[6.90,53.19]	9.80[4.60,24.20]	
Albumin (g/L)	Assumed alive	43.94[41.00,46.00]	42.00[40.00,44.00]	42.00[39.00,44.00]	<0.001	42.00[40.00,44.00]	43.00[41.00,44.00]	0.002
	Assumed deceased	43.00[41.00,45.00]	42.00[40.00,44.00]	42.00[39.00,44.00]		42.00[40.00,44.00]	43.00[41.00,44.00]	
Creatinine, urine(mg/dL)	Assumed alive	114.00[62.00,175.00]	111.00[62.00,167.00]	106.00[67.00,158.00]	<0.001	100.00[61.00,160.28]	92.00[50.00,142.00]	0.023
	Assumed deceased	99.00[55.34,154.00]	95.42[57.00,145.00]	96.00[57.00,136.00]		99.00[57.74,142.00]	91.00[50.02,137.00]	
Creatinine(umol/L)	Assumed alive	72.49[61.88,86.63]	75.14[63.65,88.40]	74.26[61.88,89.28]	<0.001	77.79[61.88,99.01]	78.68[64.53,91.94]	0.01
	Assumed deceased	79.56[63.65,91.94]	81.33[70.70,97.24]	84.86[70.70,108.23]		81.64[70.70,106.08]	79.56[61.90,97.20]	
Alanine Aminotransferase (ALT) (U/L)	Assumed alive	20.00[16.00,28.00]	22.00[17.00,31.00]	23.00[18.00,32.00]	<0.001	19.00[15.00,24.00]	20.00[17.00,26.00]	<0.001

	Assumed deceased	20.00[16.00,26.00]	20.00[16.00,25.00]	21.00[16.00,28.00]		18.00[15.00,23.00]	19.00[16.00,25.00]	
Aspartate Aminotransferase (AST) (U/L)	Assumed alive	22.00[19.00,27.00]	23.00[20.00,28.00]	23.00[19.00,28.00]	<0.001	22.00[19.00,27.00]	23.00[20.00,27.00]	0.626
	Assumed deceased	23.00[20.00,28.00]	23.00[20.00,28.00]	22.00[19.00,28.00]		23.00[20.00,28.00]	23.00[20.00,27.00]	
Alkaline Phosphatase (ALP) (U/L)	Assumed alive	64.00[53.00,78.00]	69.00[57.00,84.00]	70.00[57.00,88.00]	<0.001	70.00[57.00,86.00]	65.00[53.00,78.00]	<0.001
	Assumed deceased	72.00[59.00,90.00]	72.00[59.33,87.00]	74.00[60.00,94.00]		81.00[63.00,99.00]	75.00[61.00,91.00]	
Blood urea nitrogen (mmol/L)	Assumed alive	4.28[3.57,5.36]	4.64[3.93,6.07]	5.00[3.93,6.43]	<0.001	5.36[4.28,6.78]	5.36[4.28,6.43]	<0.001
	Assumed deceased	5.00[3.93,6.43]	5.70[4.28,7.14]	6.09[4.64,8.21]		6.10[4.64,7.50]	5.71[4.64,7.14]	
Total Calcium (mmol/L)	Assumed alive	2.35[2.30,2.42]	2.35[2.30,2.40]	2.35[2.30,2.42]	<0.001	2.35[2.30,2.40]	2.35[2.30,2.42]	0.434
	Assumed deceased	2.35[2.30,2.42]	2.38[2.30,2.42]	2.38[2.30,2.42]		2.38[2.30,2.42]	2.35[2.30,2.42]	
Bicarbonate (mmol/L)	Assumed alive	25.00[23.00,26.00]	25.00[24.00,27.00]	25.00[23.00,26.00]	<0.001	25.00[24.00,27.00]	25.00[24.00,27.00]	<0.001
	Assumed deceased	25.00[23.00,26.00]	25.00[23.00,27.00]	25.00[23.00,26.00]		25.00[23.00,26.00]	25.00[23.00,26.00]	
Gamma Glutamyl Transferase (GGT) (U/L)	Assumed alive	18.00[13.00,27.00]	22.00[16.00,33.00]	25.00[17.00,39.00]	<0.001	19.42[14.00,30.00]	19.00[15.00,26.00]	<0.001
	Assumed deceased	21.00[15.00,35.00]	22.00[16.00,33.00]	25.00[18.00,43.00]		21.00[15.00,33.84]	21.00[15.00,32.00]	
Iron (umol/L)	Assumed alive	15.58[11.60,20.06]	14.10[10.70,18.10]	13.40[10.54,17.40]	<0.001	13.14[10.40,17.20]	15.20[11.80,18.81]	<0.001
	Assumed deceased	15.20[11.60,19.70]	13.80[10.60,17.90]	13.40[10.20,17.20]		14.15[10.58,18.27]	14.87[11.46,18.98]	
Lactate Dehydrogenase (LDH) (U/L)	Assumed alive	126.00[111.00,143.00]	135.00[119.00,155.00]	131.00[115.00,152.00]	<0.001	137.00[120.00,154.00]	131.00[117.00,147.00]	<0.001
	Assumed deceased	138.00[121.00,159.00]	140.00[122.00,162.00]	140.00[121.00,164.00]		150.00[128.00,173.52]	143.00[125.00,165.00]	
Phosphorus (mmol/L)	Assumed alive	1.20[1.10,1.32]	1.20[1.07,1.32]	1.20[1.07,1.32]	<0.001	1.16[1.07,1.29]	1.19[1.07,1.29]	0.001
	Assumed deceased	1.16[1.07,1.29]	1.20[1.10,1.32]	1.20[1.07,1.32]		1.16[1.03,1.26]	1.16[1.07,1.26]	
Bilirubin,total(umol/L)	Assumed alive	10.30[8.55,13.68]	10.26[6.84,11.97]	10.26[6.84,13.68]	<0.001	10.26[8.55,13.68]	10.30[8.55,13.68]	0.071
	Assumed deceased	11.97[8.60,15.39]	10.30[8.55,13.68]	10.26[8.55,13.68]		10.30[8.55,13.68]	10.26[8.55,13.68]	
Protein,total(g/L)	Assumed alive	72.00[69.00,75.00]	71.00[68.00,74.00]	71.00[68.00,74.00]	<0.001	73.00[69.00,76.00]	70.00[67.00,73.00]	<0.001
	Assumed deceased	72.00[69.00,75.00]	71.00[68.00,75.00]	72.00[68.00,75.00]		73.96[70.00,77.00]	72.00[69.00,76.00]	
Uric acid(umol/L)	Assumed alive	309.30[249.80,368.80]	333.10[279.60,386.60]	321.20[267.70,386.60]	<0.001	321.20[267.70,380.70]	321.20[273.60,380.70]	<0.001
	Assumed deceased	321.20[267.70,386.60]	350.90[291.50,410.40]	350.90[285.50,422.30]		339.00[285.50,416.40]	333.10[279.60,404.50]	

Sodium(mmol/L)	Assumed alive	139.00[138.00,141.00]	139.00[138.00,141.00]	139.00[137.00,141.00]	<0.001	140.00[138.00,141.00]	140.00[138.00,141.00]	0.561
	Assumed deceased	139.00[138.00,141.00]	140.00[138.00,141.00]	139.00[137.00,141.00]		139.60[137.30,141.00]	139.40[138.00,141.00]	
Potassium(mmol/L)	Assumed alive	4.00[3.80,4.20]	4.00[3.80,4.20]	4.08[3.80,4.30]	<0.001	4.00[3.80,4.22]	4.00[3.80,4.30]	<0.001
	Assumed deceased	4.10[3.89,4.33]	4.10[3.90,4.40]	4.20[3.90,4.47]		4.21[3.99,4.44]	4.20[3.90,4.40]	
Chloride(mmol/L)	Assumed alive	104.00[102.00,105.00]	103.00[101.00,105.00]	102.00[100.00,104.00]	<0.001	103.00[101.31,105.00]	104.00[102.00,105.00]	<0.001
	Assumed deceased	103.00[101.00,105.00]	103.00[101.00,105.00]	102.00[99.70,104.00]		102.30[100.00,104.90]	102.39[100.10,104.92]	
Transferrin Saturation (%)	Assumed alive	24.60[18.00,32.90]	23.30[17.70,30.00]	23.21[17.00,29.19]	<0.001	22.67[17.36,28.99]	24.00[18.30,30.65]	0.573
	Assumed deceased	24.90[18.50,31.65]	23.00[17.40,30.12]	22.10[16.60,27.03]		22.80[16.60,29.50]	24.00[18.30,30.47]	
Globulin (g/L)	Assumed alive	28.00[26.00,31.00]	29.00[26.00,32.00]	30.00[27.00,33.00]	<0.001	30.00[27.00,34.00]	27.00[25.00,30.00]	<0.001
	Assumed deceased	29.00[26.00,32.00]	29.00[27.00,33.00]	30.00[27.00,34.00]		31.00[28.00,35.00]	30.00[27.00,33.00]	
alpha-carotene(umol/L)	Assumed alive	0.05[0.03,0.10]	0.05[0.03,0.10]	0.04[0.02,0.08]	<0.001	0.05[0.02,0.10]	0.08[0.04,0.13]	0.001
	Assumed deceased	0.05[0.02,0.09]	0.05[0.03,0.08]	0.04[0.02,0.07]		0.05[0.02,0.09]	0.06[0.03,0.10]	
trans-beta-carotene(umol/L)	Assumed alive	0.22[0.13,0.41]	0.23[0.13,0.41]	0.18[0.09,0.34]	<0.001	0.27[0.15,0.48]	0.37[0.22,0.56]	0.171
	Assumed deceased	0.25[0.13,0.48]	0.24[0.14,0.41]	0.20[0.11,0.35]		0.31[0.17,0.53]	0.33[0.19,0.56]	
cis-beta-carotene(umol/L)	Assumed alive	0.01[0.01,0.02]	0.01[0.01,0.02]	0.01[0.01,0.02]	<0.001	0.02[0.01,0.03]	0.02[0.01,0.03]	0.344
	Assumed deceased	0.02[0.01,0.03]	0.01[0.01,0.03]	0.01[0.01,0.02]		0.02[0.01,0.03]	0.02[0.01,0.03]	
beta-cryptoxanthin(umol/L)	Assumed alive	0.13[0.09,0.21]	0.12[0.07,0.20]	0.10[0.06,0.17]	<0.001	0.24[0.07,0.48]	0.16[0.10,0.26]	0.001
	Assumed deceased	0.12[0.07,0.19]	0.11[0.07,0.19]	0.11[0.06,0.16]		0.13[0.07,0.19]	0.14[0.09,0.21]	
Lutein and zeaxanthin(umol/L)	Assumed alive	0.25[0.18,0.36]	0.27[0.19,0.39]	0.26[0.18,0.37]	<0.001	0.33[0.19,0.45]	0.30[0.21,0.42]	0.094
	Assumed deceased	0.25[0.17,0.35]	0.24[0.17,0.34]	0.23[0.17,0.33]		0.25[0.18,0.35]	0.27[0.19,0.37]	
trans-lycopene(umol/L)	Assumed alive	0.42[0.31,0.56]	0.39[0.27,0.55]	0.35[0.25,0.51]	<0.001	0.32[0.25,0.41]	0.37[0.25,0.53]	<0.001
	Assumed deceased	0.32[0.20,0.46]	0.31[0.20,0.45]	0.30[0.18,0.45]		0.29[0.19,0.39]	0.31[0.19,0.46]	
VitaminD(nmol/L)	Assumed alive	63.10[49.20,77.70]	54.40[40.90,68.20]	54.40[39.80,68.20]	<0.001	44.40[30.20,61.10]	61.10[49.20,73.00]	0.001
	Assumed deceased	61.10[45.90,75.30]	56.30[43.40,70.54]	51.90[39.70,68.20]		58.70[44.40,70.79]	61.10[47.35,75.40]	
Creatine Phosphokinase (CPK) (IU/L)	Assumed alive	105.00[73.00,162.00]	115.00[79.00,180.00]	100.00[67.00,156.00]	<0.001	103.68[71.00,168.50]	97.00[68.00,140.00]	0.001

	Assumed deceased	95.28[62.00,140.00]	90.00[65.00,123.24]	79.12[55.00,131.36]		83.00[61.20,128.00]	89.97[61.00,128.14]	
Direct HDL-Cholesterol(mmol/L)	Assumed alive	1.37[1.11,1.66]	1.27[1.06,1.55]	1.16[0.98,1.40]	<0.001	1.27[1.09,1.55]	1.37[1.14,1.71]	0.009
	Assumed deceased	1.40[1.11,1.73]	1.29[1.06,1.55]	1.16[0.98,1.45]		1.29[1.06,1.71]	1.32[1.09,1.63]	
Direct HDL-Cholesterol (mg/dL)	Assumed alive	52.00[43.00,63.00]	49.00[41.00,59.00]	44.00[38.00,54.00]	<0.001	49.00[41.00,60.00]	53.00[44.00,66.00]	0.002
	Assumed deceased	53.00[42.00,66.00]	49.00[40.00,59.00]	44.00[37.00,54.00]		49.00[40.00,62.00]	51.00[42.00,62.00]	
Total Cholesterol(mmol/L)	Assumed alive	4.91[4.29,5.64]	5.20[4.55,5.92]	4.71[3.98,5.59]	<0.001	5.10[4.31,5.97]	5.15[4.47,5.90]	0.11
	Assumed deceased	5.22[4.50,5.95]	5.07[4.37,5.90]	4.84[4.09,5.64]		5.15[4.34,5.95]	5.28[4.60,5.92]	
Cholesterol, total (mmol/L)	Assumed alive	4.94[4.29,5.64]	5.20[4.53,5.90]	4.71[3.96,5.56]	<0.001	5.07[4.29,5.90]	5.12[4.40,5.82]	0.501
	Assumed deceased	5.20[4.47,5.95]	5.04[4.34,5.87]	4.76[4.03,5.56]		5.04[4.29,5.84]	5.17[4.53,5.84]	
Triglyceride (mg/dL)	Assumed alive	95.00[67.00,140.00]	114.00[81.00,167.00]	140.00[95.00,198.00]	<0.001	116.00[81.00,158.92]	111.00[78.00,162.00]	<0.001
	Assumed deceased	117.00[83.00,166.28]	132.00[93.00,181.00]	145.36[99.00,233.17]		118.00[81.79,178.08]	134.00[93.41,185.00]	
Triglyceride (mmol/L)	Assumed alive	1.07[0.76,1.58]	1.29[0.91,1.89]	1.58[1.07,2.23]	<0.001	1.31[0.91,1.79]	1.25[0.88,1.83]	<0.001
	Assumed deceased	1.32[0.94,1.87]	1.49[1.05,2.04]	1.64[1.12,2.63]		1.33[0.93,2.01]	1.51[1.05,2.08]	
LDL-cholesterol(mmol/L)	Assumed alive	2.90[2.33,3.49]	3.10[2.51,3.72]	2.59[2.02,3.28]	<0.001	2.92[2.38,3.60]	3.00[2.38,3.57]	0.315
	Assumed deceased	2.97[2.40,3.70]	2.90[2.33,3.59]	2.49[1.91,3.31]		2.77[2.22,3.59]	3.03[2.48,3.62]	
Glycohemoglobin(%)	Assumed alive	5.20[5.00,5.40]	5.80[5.70,6.00]	6.90[6.40,8.10]	<0.001	5.90[5.50,6.60]	5.60[5.40,6.00]	<0.001
	Assumed deceased	5.30[5.10,5.50]	5.90[5.70,6.00]	7.00[6.50,8.10]		5.70[5.40,6.30]	5.60[5.30,6.00]	
Glucose, serum (mmol/L)	Assumed alive	4.88[4.61,5.27]	5.33[4.94,5.83]	7.33[5.88,9.94]	<0.001	5.55[5.11,6.44]	5.33[4.94,6.00]	<0.001
	Assumed deceased	5.05[4.72,5.50]	5.50[5.00,6.11]	7.70[5.88,10.41]		5.55[5.05,6.56]	5.38[4.94,6.05]	
Glucose, plasma (mg/dL)	Assumed alive	95.40[89.50,101.30]	105.00[98.00,113.00]	141.00[119.00,179.36]	<0.001	106.00[98.00,123.65]	103.00[95.62,113.00]	0.019
	Assumed deceased	97.40[92.00,105.00]	107.00[98.90,116.60]	147.00[120.00,186.95]		106.94[94.19,127.66]	103.95[95.78,116.34]	
Plasma glucose: SI(mmol/L)	Assumed alive	5.30[4.97,5.63]	5.83[5.44,6.27]	7.83[6.61,9.97]	<0.001	5.88[5.44,6.86]	5.72[5.31,6.27]	0.018
	Assumed deceased	5.41[5.11,5.83]	5.94[5.49,6.48]	8.16[6.66,10.38]		5.94[5.23,7.09]	5.77[5.32,6.46]	
C-peptide:SI(nmol/L)	Assumed alive	0.65[0.49,0.88]	0.95[0.74,1.26]	1.05[0.77,1.30]	<0.001	0.95[0.73,1.12]	0.82[0.60,1.04]	0.114
	Assumed deceased	0.74[0.56,1.02]	1.03[0.77,1.38]	1.10[0.82,1.52]		0.94[0.61,1.27]	0.81[0.61,1.14]	

Insulin(uU/mL)	Assumed alive	8.23[5.46,12.78]	11.86[7.33,18.62]	14.12[8.84,23.68]	<0.001	12.02[8.20,17.43]	9.83[6.30,15.01]	0.001
	Assumed deceased	8.37[5.77,12.38]	11.41[7.04,18.33]	13.71[7.78,22.47]		10.22[6.52,15.20]	10.11[7.26,16.23]	
Insulin:SI(pmol/L)	Assumed alive	53.16[38.58,75.44]	86.49[56.40,119.88]	106.14[58.27,149.57]	<0.001	74.31[65.50,117.23]	61.81[42.40,88.56]	0.033
	Assumed deceased	53.82[38.58,72.11]	75.33[51.63,113.21]	111.93[65.64,178.06]		63.93[42.24,101.40]	58.06[42.67,91.89]	
Two Hour Glucose(OGTT)(mg/dL)	Assumed alive	99.00[82.00,120.00]	123.00[99.00,155.68]	273.75[200.00,324.99]	<0.001	139.67[118.00,192.22]	117.00[95.00,154.00]	<0.001
	Assumed deceased	122.00[97.00,152.00]	145.00[112.32,185.00]	252.70[193.18,311.31]		147.64[104.66,190.19]	139.23[114.11,166.85]	

Supplementary Table 9. Correlation analysis between common differential indicators and T2D, MCI

Terms	T2D		MCI	
	p-value	r	p-value	r
Glycohemoglobin(%)	<2.2e-16	0.8659055	<2.2e-16	0.2952395
Albumin, urine (ug/mL)	<2.2e-16	0.09745661	<2.2e-16	0.1665703
Creatinine, urine (mg/dL)	<2.2e-16	-0.04789154	8.88E-05	0.06401949
White blood cell count (1000 cells/uL)	<2.2e-16	0.1637027	1.39E-07	0.1793184
Lymphocyte percent(%)	0.0002152	0.0333719	3.04E-05	0.1167831
Lymphocyte number (1000 cells/uL)	<2.2e-16	0.2464018	2.05E-12	0.2026851
Segmented neutrophils num (1000 cells/uL)	<2.2e-16	0.1080116	5.28E-06	0.1336363
Red cell distribution width (%)	<2.2e-16	0.4641267	4.35E-14	0.2154358
Mean platelet volume (fL)	<2.2e-16	0.1681349	3.33E-10	0.212342
Folate, serum (nmol/L)	<2.2e-16	-0.2559525	3.06E-13	-0.3079924
Homocysteine(umol/L)	<2.2e-16	-0.1516209	0.008253	0.05980389
Folate, RBC (nmol/L RBC)	<2.2e-16	0.3634443	<2.2e-16	-0.1335958
Cotinine, Serum (ng/mL)	1.93E-14	-0.07875175	8.95E-13	0.2024187
gamma-tocopherol (umol/L)	<2.2e-16	0.3379875	1.12E-06	0.2623597
Retinol (umol/L)	<2.2e-16	0.226879	1.87E-08	-0.2314312
Alkaline Phosphatase (ALP) (U/L)	<2.2e-16	0.3653565	5.92E-15	0.3782906
Blood urea nitrogen (mmol/L)	<2.2e-16	0.4859246	1.00E-08	0.1939416
Gamma Glutamyl Transferase (GGT) (U/L)	<2.2e-16	0.3364554	8.97E-12	0.1932734
Glucose, serum (mmol/L)	<2.2e-16	0.4968659	3.12E-15	0.2533376
Iron (umol/L)	<2.2e-16	-0.1501646	3.17E-06	-0.1042328
Lactate Dehydrogenase (LDH) (U/L)	<2.2e-16	0.2521859	4.19E-11	0.1713453
Uric acid (umol/L)	<2.2e-16	0.3598981	1.73E-10	0.181588
Creatinine (umol/L)	<2.2e-16	0.3805017	<2.2e-16	-0.3096464

Potassium (mmol/L)	<2.2e-16	0.2247851	<2.2e-16	0.2602502
Globulin (g/L)	<2.2e-16	0.3730052	<2.2e-16	0.4330258
trans-lycopene (umol/L)	<2.2e-16	-0.2466139	5.16E-06	-0.2627177
Vitamin D (nmol/L)	<2.2e-16	-0.3782822	2.81E-09	-0.3838735
Direct HDL-Cholesterol (mg/dL)	<2.2e-16	-0.348474	1.12E-10	-0.1911604
Plasma glucose: SI(mmol/L)	<2.2e-16	0.6271029	4.05E-10	0.2789504
C-peptide: SI(nmol/L)	<2.2e-16	0.5505922	0.004511	0.165761
Insulin: SI(pmol/L)	0.007508	-0.08075077	0.01428	-0.143499
Two Hour Glucose(OGTT) (mg/dL)	<2.2e-16	0.6527652	0.001235	0.215967

Supplementary Table 10. MR analysis of indicators and T2D, MCI

Exposure	Outcome	MR method	Numbers of SNPs	β	SE	OR (95% CI)	P vale for association	P value for heterogeneity test	P value for MR-Egger intercept	P value for MR-PRESSO global test	Outlier
Red cell distribution width	Type 2 diabetes	MR Egger	18	-0.0106	0.0109	0.9895(0.9686,1.0108)	0.3442	0.7213	0.2649	0.6827	NA
		Weighted median		0.0004	0.0055	1.0004(0.9897,1.0111)	0.9456				
		Inverse variance weighted		0.0012	0.0037	1.0012(0.9940,1.0085)	0.7448				
		Simple mode		0.0012	0.0077	1.0012(0.9863,1.0164)	0.8777				
		Weighted mode		0.0012	0.0056	1.0012(0.9903,1.0122)	0.8329				
	Alzheimer's disease	MR Egger	20	0.0060	0.0076	1.0061(0.9912,1.0212)	0.4381	0.8556	0.4906	0.8943	NA
		Weighted median		0.0006	0.0045	1.0006(0.9919,1.0093)	0.8988				
		Inverse variance weighted		0.0012	0.0032	1.0012(0.9949,1.0076)	0.7134				
		Simple mode		0.0017	0.0062	1.0017(0.9896,1.0139)	0.7891				
		Weighted mode		0.0017	0.0050	1.0017(0.9918,1.0116)	0.7427				
Folate	Type 2 diabetes	MR Egger	12	-0.0200	0.0550	0.9802(0.8800,1.0917)	0.7231	0.3461	0.8517	0.4160	NA
		Weighted median		-0.0237	0.0306	0.9765(0.9197,1.0369)	0.4378				
		Inverse variance weighted		-0.0105	0.0219	0.9896(0.9480,1.0330)	0.6331				
		Simple mode		-0.0345	0.0538	0.9661(0.8694,1.0736)	0.5351				
		Weighted mode		-0.0527	0.0464	0.9486(0.8662,1.0389)	0.2795				
	Alzheimer's disease	MR Egger	14	-0.0207	0.0307	0.9795(0.9223,1.0402)	0.5120	0.1968	0.1714	0.1770	NA
		Weighted median		0.0093	0.0172	1.0094(0.9759,1.0440)	0.5884				
		Inverse variance weighted		0.0191	0.0144	1.0193(0.9911,1.0484)	0.1821				
		Simple mode		0.0376	0.0280	1.0383(0.9829,1.0968)	0.2021				
		Weighted mode		0.0076	0.0176	1.0076(0.9735,1.0429)	0.6728				
Gamma tocopherol	Type 2 diabetes	MR Egger	67	0.0400	0.0574	1.0408(0.9301,1.1647)	0.4881	0.0044	0.2814	0.0030	NA
		Weighted median		-0.0300	0.0489	0.9705(0.8818,1.0680)	0.5396				

		Inverse variance weighted		-0.0113	0.0325	0.9887(0.9276,1.0538)	0.7274				
		Simple mode		-0.1620	0.0969	0.8504(0.7033,1.0284)	0.0994				
		Weighted mode		-0.0323	0.0515	0.9682(0.8752,1.0710)	0.5321				
	Alzheimer's disease	MR Egger	65	0.0029	0.0394	1.0029(0.9284,1.0835)	0.9410	0.0930	0.5989	0.1120	NA
		Weighted median		0.0003	0.0366	1.0003(0.9311,1.0748)	0.9925				
		Inverse variance weighted		0.0189	0.0251	1.0191(0.9702,1.0705)	0.4507				
		Simple mode		0.0313	0.0689	1.0318(0.9015,1.0685)	0.6513				
		Weighted mode		-0.0021	0.0349	0.9979(0.9319,1.0685)	0.9514				
Alkaline Phosphatase	Type 2 diabetes	MR Egger	121	0.0496	0.0434	1.0508(0.9652,1.1441)	0.2553	5.46E-08	0.1314	<0.0003	rs12133641 rs645040
		Weighted median		-0.0009	0.0321	0.9991(0.9381,1.0640)	0.9777				
		Inverse variance weighted		-0.0048	0.0246	0.9952(0.9483,1.0445)	0.8458				
		Simple mode		-0.0574	0.0655	0.9442(0.8304,1.0735)	0.3822				
		Weighted mode		0.0186	0.0339	1.0188(0.9553,1.0887)	0.5837				
	Alzheimer's disease	MR Egger	132	-0.0120	0.0252	0.9881(0.9404,1.0382)	0.6352	0.0624	0.2598	0.0620	NA
		Weighted median		-0.0020	0.0231	0.9980(0.9538,1.0442)	0.9312				
		Inverse variance weighted		0.0102	0.0159	1.0103(0.9793,1.0422)	0.5197				
		Simple mode		-0.0082	0.0368	0.9918(0.9228,1.0659)	0.8233				
		Weighted mode		0.0020	0.0213	1.0020(0.9610,1.0448)	0.9240				
Blood urea nitrogen	Type 2 diabetes	MR Egger	121	-0.2062	0.3449	0.8136(0.4139,1.5995)	0.5510	7.78E-11	0.7064	<0.0003	NA
		Weighted median		-0.1807	0.1843	0.8347(0.5816,1.1979)	0.3269				
		Inverse variance weighted		-0.3246	0.1432	0.7228(0.5459,0.9571)	0.0234				
		Simple mode		0.2656	0.6491	1.3042(0.3654,4.6544)	0.6832				
		Weighted mode		0.2073	0.4728	1.2304(0.4871,3.1083)	0.6618				
	Alzheimer's disease	MR Egger	134	-0.3150	0.2217	0.7298(0.4726,1.1270)	0.1577	0.0794	0.0816	0.0683	NA
		Weighted median		-0.1152	0.1508	0.8912(0.6631,1.1977)	0.4451				
		Inverse variance weighted		0.0318	0.1012	1.0323(0.8465,1.2588)	0.7535				

		Simple mode		0.1130	0.3045	1.1197(0.6164,2.0338)	0.7111				
		Weighted mode		-0.0779	0.1955	0.9251(0.6306,1.3572)	0.6911				
Gamma Glutamyl Transferase	Type 2 diabetes	MR Egger	118	0.0554	0.0422	1.0570(0.9732,1.1481)	0.1910	1.27E-07	0.9716	<0.0003	rs28360467 rs4298983
		Weighted median		0.0378	0.0283	1.0385(0.9825,1.0976)	0.1813				
		Inverse variance weighted		0.0542	0.0215	1.0556(1.0122,1.1010)	0.0116				
		Simple mode		0.1900	0.0724	1.2093(1.0493,1.3936)	0.0098				
		Weighted mode		0.0556	0.0361	1.0572(0.9849,1.1347)	0.1264				
	Alzheimer's disease	MR Egger	120	-0.0137	0.0195	0.9863(0.9494,1.0247)	0.4816	0.0010	0.8842	0.0013	NA
		Weighted median		-0.0043	0.0167	0.9957(0.9637,1.0288)	0.7975				
		Inverse variance weighted		-0.0116	0.0124	0.9885(0.9647,1.0129)	0.3516				
		Simple mode		-0.0232	0.0327	0.9770(0.9164,1.0416)	0.4781				
		Weighted mode		-0.0191	0.0146	0.9810(0.9535,1.0094)	0.1912				
Urea Acid	Type 2 diabetes	MR Egger	124	0.0568	0.0297	1.0584(0.9986,1.1217)	0.0580	3.77E-06	0.0351	<0.0003	rs9895661
		Weighted median		0.0322	0.0255	1.0328(0.9824,1.0857)	0.2058				
		Inverse variance weighted		0.0084	0.0194	1.0085(0.9709,1.0475)	0.6637				
		Simple mode		0.0445	0.0505	1.0455(0.9469,1.1543)	0.3808				
		Weighted mode		0.0233	0.0258	1.0236(0.9732,1.0766)	0.3667				
	Alzheimer's disease	MR Egger	116	-0.0285	0.0132	0.9719(0.9471,0.9975)	0.0336	0.2753	0.1621	0.2540	NA
		Weighted median		-0.0193	0.0132	0.9809(0.9558,1.0066)	0.1430				
		Inverse variance weighted		-0.0150	0.0092	0.9851(0.9675,1.0030)	0.1024				
		Simple mode		0.0032	0.0203	1.0032(0.9640,1.0440)	0.8758				
		Weighted mode		-0.0181	0.0116	0.9821(0.9600,1.0047)	0.1219				
Creatinine	Type 2 diabetes	MR Egger	72	-0.0323	0.1540	0.9682(0.7159,1.3094)	0.8343	1.64961E-06	0.7507	<0.0003	rs9895661 rs11924016
		Weighted median		-0.0340	0.0522	0.9666(0.8726,1.0708)	0.5155				
		Inverse variance weighted		-0.0795	0.0430	0.9236(0.8490,1.0047)	0.0642				
		Simple mode		0.0798	0.1152	1.0831(0.8641,1.3576)	0.4908				

		Weighted mode		0.0432	0.0900	1.0442(0.8753,1.2456)	0.6326				
	Alzheimer's disease	MR Egger	76	-0.0373	0.1472	0.9634(0.7219,1.2856)	0.8005	0.0113	0.5549	0.0153	NA
		Weighted median		0.0465	0.0537	1.0476(0.9429,1.1639)	0.3865				
		Inverse variance weighted		0.0465	0.0409	1.0476(0.9669,1.1351)	0.2558				
		Simple mode		0.1584	0.1478	1.1716(0.8771,1.5652)	0.2871				
		Weighted mode		0.1411	0.1459	1.1516(0.8651,1.5329)	0.3365				
Globulin	Type 2 diabetes	MR Egger	7	0.0219	0.0427	1.0222(0.9400,1.1115)	0.6297	0.2963	0.7426	0.4580	NA
		Weighted median		0.0020	0.0104	1.0020(0.9818,1.0227)	0.8450				
		Inverse variance weighted		0.0074	0.0083	1.0075(0.9912,1.0240)	0.3714				
		Simple mode		0.0022	0.0173	1.0022(0.9689,1.0366)	0.9036				
		Weighted mode		0.0016	0.0168	1.0016(0.9692,1.0351)	0.9266				
	Alzheimer's disease	MR Egger	8	-0.0030	0.0214	0.9970(0.9561,1.0396)	0.8919	0.0794	0.0816	0.0683	NA
		Weighted median		0.0071	0.0067	1.0071(0.9940,1.0204)	0.2890				
		Inverse variance weighted		0.0053	0.0054	1.0054(0.9948,1.0160)	0.3212				
		Simple mode		0.0066	0.0092	1.0066(0.9886,1.0250)	0.4968				
		Weighted mode		0.0079	0.0085	1.0079(0.9912,1.0249)	0.3866				
Vitamin D	Type 2 diabetes	MR Egger	105	-0.0971	0.0504	0.9074(0.8221,1.0016)	0.0567	0.0013	0.2383	0.0017	NA
		Weighted median		-0.0687	0.0403	0.9336(0.8627,1.0103)	0.0881				
		Inverse variance weighted		-0.0488	0.0297	0.9524(0.8986,1.0094)	0.1003				
		Simple mode		-0.0560	0.0939	0.9455(0.7866,1.1366)	0.5523				
		Weighted mode		-0.0700	0.0411	0.9324(0.8602,1.0107)	0.0920				
	Alzheimer's disease	MR Egger	109	-0.0167	0.0303	0.9835(0.9268,1.0436)	0.5830	0.7138	0.8073	0.7573	NA
		Weighted median		-0.0174	0.0274	0.9828(0.9314,1.0370)	0.5258				
		Inverse variance weighted		-0.0106	0.0174	0.9894(0.9563,1.0238)	0.5420				
		Simple mode		0.0310	0.0469	1.0314(0.9409,1.1308)	0.5105				
		Weighted mode		-0.0160	0.0286	0.9841(0.9305,1.0408)	0.5770				

Supplementary Table 11. Gene list

	Gene	Number
ND-T2D up-regulated Degs	SLC9A3, RPS4Y1, B2M, NDUFB7, EIF5, ADAM15, GNAQ, S100A9, PTPRC, RP2, IREB2, HLA-A, GABPA, EIF1AY, HERC3, EEF1A1, JAK1, UBE2E3, ABHD3, CASC4, CHURC1, PRKY, STXBP3, FBXO9, LYPLA1, MORC3, SLC23A2, EFNA4, TRIM23, MTHFS, LRRN3, ITGA4, CNTNAP2, PDE4D, GNG10, KCNJ4, PPM1A, PRDX3, MCTP2, GNG2, DMXL2, APP, CLASP2, DCK, TMF1, CSF2RB, SLC4A1, SNCA, HEMGN, MICAL2, FBXO3, WDR47, ADAM10, CAPN7, MBNL3, TNFAIP8, FBXO7, EPC1, CCNG2, RBL2, CA2, ENPP4, ITPR2, TAF2, RAB4A, HLA-DQA1, PIK3CB, AGPAT5, SLC25A36, MTM1, CACYBP, HLA-DQB1, FUBP3, ARL6IP6, OTUD4, CD2AP, ORM1, DR1, ESPN, NAT1, RWDD3, BTF3L4, SDHD, CASP8, ARRDC3, THBS1, IRX3, MAP7, AKAP10, COMMD8, CPEB4, CRLF3, ARF4, OSBP2, RSRC1, CSNK1G3, E2F5, ADIPOR1, HIF1A, PIK3C2A, SDCBP, GPR146, YPEL2, HIST1H3F, STEAP4, JMJD1C, NUP160, SCML1, CCNT2, AFF4, PPWD1, RPS18, MCEE, BANK1, ZNF217, RPE, CHORDC1, TRIM58, CD58, TM6SF1, KLHL20, BTBD1, RAB5A, CDC42, PDE3B, POLR2J2, HIST3H2A, GNPDA2, CPEB2, ITGAV, STRN3, EP300, XK, DNAJA4, HPS3, LRRK2, CCNC, CHMP1B, SMARCAD1, RPS12, RGS18, OSBPL10, TSPAN13, BET1, ANAPC1, LIPT1, CD9, COMMD10, CHMP2B, MDFIC, PDE7A, MORF4L2, TNRC6C, G3BP2, NBR1, CLK1, CACNA2D3, CXCR4, DPM1, TTF2, ATP7A, CD46, PTPN12, NUDT21, DYRK1A, PHC3, P2RY13, CHI3L1, TIA1, ID3, RPGR, FNDC3A, GPR34, CCNDBP1, SNX10, STX7, FNTA, SPAG9, NFIA, SESN3, RPL7, AASDHPPT, RCHY1, BTF3, AP3S1, ADCY7, STAG2, PCNP, MGAM, GLCCI1, TSC22D2, YTHDC2, FBLN2, NR2C2, GIT2, STT3B, OGFRL1, RCN2, TMEM106B, DDX21, LCP2, ITGB3BP, NRBF2, SRI, USP22, CD55, ARHGAP12, FCER1A, RAB3IL1, GNG11, RPS6KA5, DPYD, TGFBR2, TMEM41A, ATG4B, ZNF654, PIGB, ZDHHC2, RPL41, ACP5, SOCS4, PSMD10, UCHL5, LGALS3, TAGAP, CNOT7, PLAG1, YME1L1, ANKRA2, SLC16A10, CYB5R4, KLRC1	232
ND-T2D down-regulated Degs	KPTN, ST14, MAP2K7, MT2A, CACNA1I, NTHL1, GTF3C5, TTC12, ILVBL, SLC22A17, ZNF282, CEP164, RIMS3, RNF40, FAM98C, GZMH, RAB4B, MVD, TMC6, ALDH16A1, TRMU, SMARCD3, GHRL, MUS81, PLEKHB1, SPIN1, CIC, MRPL28, PARP14, DCTN5, ARMC7, PPP1R13B, ITGA2B, RRAS, OAS1, CAPNS1, VAC14, RPS6KA4, YPEL4, NUAK1, GIPC1, TUBGCP2, TMEM62, TSEN54, REXO1, WDR5, CHD3, POLD2, IL2RG, GPR68, CROCC, SLC25A11, CEP250, INPPL1, NOXA1, DDX41, GSN, MPO, OASL, GPI, CHRNA10, OS9, IKBKE, WDR46, TTYH3, PRKCSH, SLC5A3, ZNF408, MAP3K11, SLC25A1, DYSF, RGL1, DRD3, ADCK5, DAXX, GLYCTK, DRG2, ABCA2, MFN2, OAS2, MVP, AGTRAP, NCOR2, DDB2, S100A13, FOSB, PRKD2, TJP3, NEK6, WDR25, PEX26, PELP1, CASP5, RNASET2, SIL1, CBFA2T3, FOXD2, CLEC4D, BOP1, SMG7, RNF157, RSAD1, CD300LB, MT1E, ITGAL, LAP3, VPS39, SH3PXD2A, RGPD1, SIGLEC5, DPP7, ANKDD1A, CACNA1E, LRRC45, GMIP, PPP2R5D, ABHD14B, SLC9A8, DLG4, TBRG4, H1FX, ENO2, PKN1, TNFAIP6, POU2F1, TSPYL2, HP, RTP4, BAK1, ANKRD33, POLD1, POLRMT, POU2F2, MX2, TUBG2, PEX14, FAM20C, ENTPD6, CTSW, CSRP1, SERGEF, DDX6, ABCF3, DTX3, RIN3, PAFAH1B3, PYGO2, OSBPL5, VPS13D, SH3TC1, SFXN5, TBC1D17, MC1R, TCN1, IFIT5, CD3E, HEY1, H1F0, SFI1, DBP, CROT, CXCR3, TRIM46, COL9A2, ZDHHC24, AATF, CRTC2, COX15, AGPAT4, BCL7C, KIAA0100, HAPLN3, ARHGAP10, OTUD5, MYO1G, SHKBP1, PMF1,	320

	BATF2, CDKN1A, APOL3, SEMA4A, ICAM1, CITED4, PLXNB2, NCR3, MAN2B1, ITM2C, SLC26A8, GSS, HRAS, GPAA1, RNF31, DNHD1, MAN2C1, PDZD4, LAMP3, MBD3, SUPT5H, GMPPA, DGCR8, CCDC22, ZNF683, NAGA, ATXN3, B3GAT3, MOV10, ATG16L2, LRP1, SIRPB1, RRBP1, AHNAK, PTPN6, TFEB, SSBP3, AKAP8L, RTBDN, KIF13B, COL6A2, RAB11FIP5, MRPL2, EPHB1, SAMD9L, GIT1, LAIR2, ASPSCR1, GDPD5, ZNF580, SUPT6H, RPIA, RPUSD1, TRAF2, SCO2, CD320, PLOD3, UQCRC1, SP1, UNC5C, ENG, MXRA7, DLGAP4, DBN1, ATP13A1, EIF2AK2, TTC21A, MARCO, TBCD, SLC4A2, G6PC3, IFIT1, VPS4A, MGRN1, HLA-G, ABCD1, NDUFB11, TMEM107, RNF26, CAPN3, SGTA, GTF2E1, VPS18, LAG3, IFI35, PI3, PDGFRB, TBC1D10B, CHTF18, HAPLN2, SYMPK, TOR2A, RAB11FIP4, EPHB6, PARP12, PRSS21, HERC6, HES4, DCP1B, EPSTI1, GADD45G, NCF4, FGFRL1, PLXNA3, PCBP4, ERBB2, XIST, LGALS9, TAF6L, FANCG, QDPR, ASGR2, PDK4, FAM78A, ACADS, ARFGAP1, VAMP5, OGFR, APOL1, OAS3, IFI44, APOBEC3D, HERC5, CALCOCO1, IDH2, RFNG, LGALS3BP, LY6E, RNASE3, MX1, IRF7, STK11, TNFSF12, PRMT7, OTOF, SERPING1, DYNLRB1, RSAD2, RAMP2, IFI44L, MMAB, HBG1, ZDHHC8	
MR SNPs Gene	CSGALNACT1, BICRA, Y_RNA, GLULP3, MARCHF8, ETV5, CETP, PDXDC1, LOC105372112, LOC105379311, NUP93, ABCA1, LINC02702, DNAH10, GPAM, LOC105375091, APOA1-AS, LOC105371632, RGS17, RPL35AP19, RPL30P9, TET2-AS1, BUD13, LPL, ALDH1A2, KNTC1, TP53BP1, YDJC, CYP26A1, LIPC, GALNT2, STARD3NL, APOC3, BBS2, PRAM1, NLRC5, TRIB1AL, IRF2BP1, APOC1P1, SLC12A3, NUP93-DT, AFF1, GNAO1, TTC39B, PGS1, NFIA, TRIP11, PLTP, LOC107984372, SCARB1, GIMAP6, SNX13, CELSR2, LOC105370050, SIK3, RPL19P16, PLEKHG3, PSME3IP1, ZNF664, PSKH1, DOCK6, CYCSP55, LIPG, LOC105369688, SEC14L4, ZPR1, STAB1, HERPUD1, FNBP1L, UBASH3B, RRN3, LINC02151, LOC105370044, RNA5SP224, SNTB1, INTS10, NIP7P1, TRGC2, FOXA3, APOC4, LOC124903363, PCIF1, WDR11, NUP50P1, RSPRY1, ZNF664-RFLNA, LIPC-AS1, LOC105371287, KRT18P9	89
GeneCards Gene	APOA1, ABCA1, CETP, LIPC, LCAT, APOE, LPL, APOB, APOC3, SCARB1, ALB, APOA1-AS, ANGPTL3, LDLR, INS, NIPSNAP3B, PPARG, CRP, APOA5, PON1, TP53, POLR2A, TNF, ADIPOQ, APOA2, IL6, LIPG, GBA1, LINC01672, POLR3A, LEP, GALNT2, APOA4, SLC12A4, LPA, PLTP, PPARA, CREB3L3, SMPD1, POLD1, MTTP, POLG2, F2, IGF1, ACE, IL10, ABCG5, AR, LMNA, APOC2, LIPE, EGFR, CBS, PCSK9, SERPINE1, PTEN, F3, FBN1, AKT1, ESR1, CERNA3, HNF1A, ABCB11, IL1B, LIPA, TLR4, IL4, DOCK7, BRCA2, MAPK1, RB1, GPT, CTNNB1, IFNG, NFKB1, FAS, H19, SELP, APP, CFTR, TMX2-CTNND1, INSR, CAV1, HMGCR, SOD1, NF1, TGFB1, MIR7-3HG, LEPR, PSEN1, VEGFA, PTPN11, NR1H2, PLAT, VDR, ICAM1, NPC1, MECP2, SLC25A13, CXCL8, JUN, FGFR2, ABCG8, SELE, ABCB1, CTSD, PRKN, FGFR1, KDR, NOS3, IL13, ABCG1, EP300, CD36, ADRB2, TTR, IFT74, CSNK2A1, F8, SP1, MSH6, F10, SPP1, STAT3, BBS1, SNCA, BCL2, IRS1, SCARB2, XIST, POMC, CEP290, BBS7, MMP2, ABCA4, BBS2, HBB, IDUA, LOC106627981, SHBG, MAPK14, RELA, COL5A1, PLCG1, RAF1, MTHFR, CLU, IFT172, SERPINC1, GCK, KIF3B, RETN, ALMS1, TF, ABCA7, VWF, IL2, GRB2, BBS10, SMAD4, CDKN1A, CEP19, FGF2, KIF3A, PPARD, COG2, BAX, HRAS, PIK3R1, WDPCP, CCL2, CD40LG, SCAPER, KIF5B, MMP9, ATM, IFNA1, TNFRSF1A, HLA-DRB1, EGF, PARK7, IL2RA, IL18, NPHP1, SCLT1, PLA2G6, PAFAH1B1, TCF4, TTC39B, PARP1, GGT1, NR3C1, AVP, PRL, HNF4A,	2598

	HSP90AA1, CASP3, HMOX1, SMARCA4, SREBF2, GHR, MKKS, SDCCAG8, PPARGC1A, GPIHBP1, MEFV, HTR2A, SFTA3, COMT, VCP, STAT1, CNR1, REN, IFT27, UCP1, YY1, RXRA, PRKCD, CDKL5, TRIM32, SLC17A5, PTGS2, LINC02605, IGFBP3, TGFBR2, HIF1A, BMP4, CTLA4, NR1H3, MAPK3, CXCR4, APC, BBS4, PDGFRB, ABCC6, GLA, MVK, MPO, ENG, NR1H4, BCHE, OXA1L, NPPB, FGFR3, BBS5, HFE, CCR5, TTC8, CDKN2A, F9, TERT, CDK5, TLR2, BIRC5, CREB1, DLG4, ANGPTL8, CYP17A1, EPO, ITGB3, GATA4, PIK3CG, ITGAM, MEG3, GLB1, ADA, MALAT1, MC4R, TARDBP, BGLAP, IGF2, SERPINA1, ESR2, BTK, MKS1, MAPK8, CCL5, IL17A, MT-CO1, ARF1, CDK4, GP6, BLM, MMP1, BBIP1, MTOR, CFAP418, DNASE1, CYP19A1, C3, MET, CASR, AGT, MAP2K1, HGF, F5, CREBBP, DIABLO, IL1A, SCN5A, TTN, PTCH1, CAT, IL5, ANGPTL4, CYP3A4, CD79A, CD40, ELANE, PSMB8, RHO, TNFAIP3, G6PD, AP3B1, PRKCA, ALOX5, ARL6, IRF5, GHRL, JAG1, AGTR1, CXCL10, ACE2, BBS9, FLT4, ELN, FABP4, NAMPT, AFP, RPL36A-HNRNPH2, BBS12, BDNF, TLR8, CYP1A2, IDS, MIR21, LZTFL1, ABCB4, GSTM1, ACTB, APOC1, NOD2, MSMO1, FADS1, NOS2, DYRK1A, GNRH1, CYP27A1, IGF1R, CASP8, CCND1, XIAP, RHOA, NPPA, SAR1B, KDM6A, FABP2, ATP7B, LTF, TIMP1, FEN1, GJA1, FOS, VCAM1, SLC7A7, NPHS1, UBC, COL3A1, TGFBR1, ARSA, TLR7, CBL, GSK3B, PLIN1, MYO6, GJA5, CTCF, CES1, UBE2L3, AKT2, SLC6A4, KCNH2, NDE1, JAK2, NR2E3, NKX2-5, GCKR, SHC1, GALC, XRCC6, VTN, FLNA, FCGR2A, PINK1, ATRIP, SYT1, PIK3CA, CX3CL1, MEF2C, SIRT1, SGMS2, PAH, PRKAB1, IRAK1, HERPUD1, CASP1, FTO, RAB11A, GH1, RHOD, THBD, RNASEL, CHUK, HDAC1, TNFRSF1B, SMAD5-AS1, GCOM1, RFC1, CALCA, F7, PLA2G7, ITGB1, CUBN, LRRK2, VHL, IRF3, PRKCB, LIF, TGFA, TH, CCL3, IFT52, CSF3, ASL, APOH, GUCY2D, FLT1, WWOX, CSF2, SH2D1A, BID, CSNK2A2, GCG, DRD2, TYRP1, PON3, GATA6, RAG1, ABCC8, SQSTM1, HDAC2, NFKBIA, SREBF1, PSAP, MCL1, PLAU, TOP1, EZR, HEXA, PALB2, CCK, PRKACA, ADH1C, HOTAIR, STX1A, KAT5, DMD, CYP1B1, SLC3A1, COL4A1, TERC, GUSB, SMARCB1, BCL6, TRAF6, GSTT1, GSTP1, IFNB1, IL3, NR3C2, CACNA1F, APBB1, B2M, KNG1, ACHE, CP, CSNK2B, ITGA2, MED1, IL1R1, CIDEC, FN1, MT-TL1, LAMP1, OFD1, CASP9, CD44, USF1, LIPE-AS1, ISG15, ADRA2A, GRN, MSH3, FLNC, CFH, FCGR3B, MMAB, NFE2L2, CCL11, SLC6A2, FYN, E2F4, SOCS1, MPZ, OTC, BSCL2, FOXC1, NR4A2, HADHA, DPP4, ADRB3, PGR, GATA2, EDN1, SMARCA2, KIF17, CACNA1C, ADRB1, FURIN, PTGS1, PTPN22, DHFR, NPC2, LAMP2, KCTD10, TRA, CELA2A, TXN, SETD2, FAH, PON2, VIM, HLA-B, KCNJ2, DCTN1, ITIH4, LMF1, MYD88, HP, NTRK1, COL1A1, NEK1, RARA, RPL10, IL2RB, SLCO1B1, TYMS, UCP3, KAT2B, P4HB, DRD4, MAOB, VAMP2, BDKRB2, TUBG1, CSF1, FANCA, PITX2, PRKD1, MIR320A, KCNJ11, ABCA13, IL1RN, PBX1, SOAT1, ABCC1, OPRM1, BMP2, TBX5, PRTN3, PGR-AS1, NPY, OAT, ANK2, UBE2I, SOD2-OT1, SGMS1, RBP4, TNFRSF11B, EEF1A1, BAZ1B, CYP2D6, TNFRSF10A, DCN, ITGA2B, PRKCZ, RUNX2, PRKAA1, APTX, TSC1, SELL, RUNX1, VPS35, RXRG, HSP90AB1, BAK1, TNFSF10, VLDLR, SST, GLI2, MYH11, NCOA1, SFTPD, NLRP3, HSPA8, MIR140, F2R, PLAUR, FCGR3A, MGMT, TPM1, HCAR3, HSPG2, TFRC, EPC1, ACP1, APOC4, FGA, ZMPSTE24, ABCG4, ERCC4, HLA-DPB1, IGFBP1, HNRNPH2, CARM1, GC, EPAS1, PF4, MED27, ESRRB, CPLANE1, ITGAL, GNAS, CANT1, FOXO1, SHH, PCYT1A, PROC, RNASE3, DHCR24, PLG, TCF20, ITGAV, ANXA5, PTPN1, KITLG, NUP93, LBR, BRIP1,	

	PLEK, MED23, ANXA2, TPO, CIITA, CSTB, CCN1, ERCC2, PAXX, C4B, DDB2, TFAM, SLC2A4, SRD5A2, SLC22A5, XPR1, TAP1, DUSP1, SUMO1, ABCB7, KAT7, PKD1, IGHE, CITED2, GAA, RBBP4, VCL, ANPEP, PWAR1, RPS19, NRG1, USH2A, ATP13A2, TGFB2, MT-CYB, FOLH1, AKR1B1, CNTNAP2, NCOR2, PIK3C2A, PRKAA2, CYP2C9, CRKL, SOD2, LIG1, FANCC, PPT1, PTH1R, CST3, TNNT2, MAOA, PRF1, CXCL12, FANCG, GLUD1, LEPQTL1, ASAH1, ANGPT2, SOCS3, KLK3, ENPP1, RIPK1, TMPO, TLR5, RPL18, ALPL, CDKN1B, PCSK6, ATF2, ZNF202, HLA-G, RPLP2, CALM1, THRB, APAF1, CAVIN1, TNFRSF10B, ABCA12, CYP1A1, RNF216, PVT1, CYP7A1, STXBP2, BACE1, COL1A2, FADS2, CEBPB, MIF, GLI1, FANCM, RECK, MEN1, OCRL, DICER1, RAD9A, NOTCH2, SI, IGBP1, CETN2, KRT18, KCNQ1, NDEL1, MLXIPL, HADHB, TOP2B, RFC3, SLC11A1, SLC19A1, HSPD1, PTK2B, EDNRA, CSN1S1, SPTAN1, MT-TP, ODC1, TPP1, LRP5, FLCN, CEBPA, PPP2R2B, GPHN, TCF7L2, XRCC2, ITGB2, JAK1, PKHD1, IGF2R, CDK20, SFTPB, CYP2C19, TOMM40, CMA1, IL7, RFC4, CRX, LBP, NAT2, DISC1, CYBA, RAB10, DYNC1I1, LTA, IL6ST, RPE65, ALDH2, CALR, UBE3B, COL4A5, PDX1, SAA1, EXOC7, ABCG2, FUT2, PNLIP, LMO7, LRP1, STX11, PLCB1, RFX1, SLC12A3, PECAM1, ARSB, TRIB1, DSP, PKD2, CDK6, VPS13B, IGFBP2, THPO, MAF, ADORA2A, GRK2, NPC1L1, MGAM, L1CAM, PLA2G2A, UNC13D, ALDOB, DYNLL1, LACTB, BIRC2, GNAI2, PRDM16, TIMP2, IL12A, THBS1, GPX1, NTRK2, USP9X, TRPS1, LIPF, SNRPN, IFT81, HSD3B2, GP1BA, LOX, STAT5A, FSHR, CAMK2G, LGALS3, SOS1, DVL1, SYNE2, SERPINA3, APOD, HMBS, FASN, WRN, CYP2E1, DGUOK, DNM3, MIR27A, PDPK1, XRCC1, ASTN2, HMGCL, FOXA2, LDLRAP1, ARF4, SLC1A3, LGALS3BP, SUN1, NECTIN2, PCCA, MTA1, CLCN1, NPPC, TLR9, NRAS, CSK, MME, S100A8, SRSF6, IL15, ADM, CYP27B1, MIR30A, BSG, DHCR7, MBL2, ELK1, LMNB1, HRH1, KMT2C, DRD1, ACVRL1, CTSG, HULC, CHIT1, PAX2, SCNN1B, TRPV1, ELAVL1, ACTN4, IL12B, AGPAT2, NQO1, AQP1, RPGR, WDR35, PDZK1, KIDINS220, HTR2B, SLC4A1, NLRP1, CD163, MAP3K5, HNRNPA1, CTSS, MCOLN1, CRAT, SRF, MYB, IFT140, PCSK1, IL18R1, ASS1, BIRC3, SATB2, SORL1, HSPA1A, CEP104, UCP2, ABCA3, MMP3, AXIN1, LMNB2, SLC7A5, SLC3A2, GSR, PKN2, IL1RAPL2, PSEN2, ALPP, PAX3, NR1I2, PLA2G4A, DKK1, ALAD, CRK, MIR125A, AUTS2, PLEC, CRABP2, TRIM21, MYBPC3, DUSP6, POR, C4A, CSF2RA, PTGIR, TAC1, GLI3, EIF3A, PCNT, DNM2, CD14, EPHX2, CPS1, SAA4, PIK3CD, NIN, CCR2, GSN, PEPD, CPT2, BMAL1, NAXE, JAZF1, SURF1, MIR155, MMP14, TNFSF4, NCAM1, MYO7A, TFEB, PTH, CYLD, STAT2, ACADVL, PRPF31, GLP1R, NAGS, EIF2A, DES, FGF23, CD86, IFNAR1, CKM, P2RY12, CTSB, ITGB4, SUMO3, ATF3, NOS1, STAT6, ADCY10, IFIH1, PIK3CB, COL4A2, GM2A, UGT1A1, PSIP1, TNFSF11, DAB1, FGB, CASP7, AGER, RPS6KB1, WHRN, CHAT, OSM, MAP3K1, SULT1A3, FXN, PKLR, EVC2, SH2B1, PITPNA, NOD1, SRD5A1, KIAA0319L, HBEGF, BCL2A1, HPGD, SLC16A1, EXT2, ADAM17, TRD-GTC9-1, BTG2, RYR2, FKTN, MRC1, ITGA4, SDHB, PTPN3, LTA4H, RBM5, PTHLH, NAT1, ERBB3, VANGL2, ACP5, SNAPIN, FLT3, ADD1, TMEM209, PRKAG2, ZNF568, SERPINA7, KLC1, CGB5, PDGFRA, HLA-DRA, F2RL1, MIR33A, PLD2, REST, DYNC2LI1, FOXP2, NR2F2, MIR146A, TYMP, NCOA3, SLC25A15, SORT1, BHMT, KIFAP3, GRB10, IAPP, VAV1, PPBP, IRAK4, PDGFB, DYNC2H1, ACADM, ADGRV1, HTR3A, PI4KA, LYST, USH1G, OPA3, PRKAG1, IL4R, RORA, UBIAD1, PARP2, SLC9A3, TNFRSF10D, GABBR1, OGG1, ACACA, NEK9,	

	PLCG2, SOAT2, GCH1, TTF2, ANGPT1, PDE2A, SERPINF1, PRKG1, FBL, HBA1, TBXA2R, DNAH10, PROS1, PLIN2, PRKCQ, SERPINB2, PIAS1, CPE, PARD3, BPI, TRH, ADH1B, FUZ, THBS4, SLIT2, IRS2, SKP2, HSD11B1, CTNNA1, EXOSC4, AP2M1, IDO1, MIR34C, STAR, RXRB, RAB5A, JAK3, CPA6, IDE, CLN3, MAPK7, TMEM67, STX5, EMD, DRD3, ANXA1, LGALS1, CCL18, NODAL, NCOR1, MAPK12, MYBL2, ILK, PRPF8, RARB, GDF15, SLC4A4, PRKCG, RHCE, ERBB4, THOC5, F13A1, GAL, MAGT1, ACTA2, ESRRG, TRIM22, BCL11A, GRM1, CDH5, NOTCH3, SPARC, ALDH1A2, AMH, EPHX1, MOG, HDAC4, FLOT1, KL, CNTF, G6PC1, ACTL6B, GLUL, FARS2, ARNT, CXCR2, BRPF1, C9orf72, STAT5B, DBH, TRAF3, ARG1, ACTC1, GJA4, ABCA2, BMPR2, IKZF1, CCKBR, RCN2, UGCG, MIRLET7C, RAB27A, IL6R, NAGLU, RAB8A, KIF7, DUSP5, GRK1, MYH3, SLC10A2, ACAN, COL2A1, SPINK1, HCFC1, PCDH15, DDC, INSIG2, SKIC2, SELPLG, MAP2K6, MMP13, HLA-DQA1, HDAC9, UBE2C, INS-IGF2, RPGRIP1L, MAPK11, EDNRB, RICTOR, FOXO3, SLC12A1, PSMD1, TFPI, PLD1, IFT122, GABRA1, HNRNPUL2-BSCL2, GAD2, CEP120, TCTN3, RMI1, CFLAR, APOL1, GNAI1, TAL1, WFS1, ADORA1, PMAIP1, NR1I3, HEXB, SMO, ATP2A2, PRKAB2, IKBKE, DNAH11, CAMP, PICK1, ISCA2, NPHP4, PDE3A, DDX39B, SLC25A11, GNB3, ACD, PABPC4, FAAH, SARM1, FKBP1A, CIC, SLC7A6OS, C5, RACGAP1, TMEM237, APOF, PEX14, EYS, CAMTA1, PTGIS, ADRA1B, NCF2, ACADS, RIPK2, AGRP, NPR2, ATG5, AHCY, WNK1, C1QBP, F12, PPP1R3A, PXK, DGCR5, GAD1, PLCD1, XPO5, NUTF2, INVS, USF2, SPRED1, PPP1R9A, MEF2A, FHL1, IRF8, CFB, IFT43, CLTC, ADAMTSL1, ASPA, SPRY4, RHCG, WDR19, PCK2, ERN1, HTRA1, RNF8, PIK3R2, CLOCK, DYNLT1, DYNLT2B, ARL13B, TXNIP, MYOF, CXCR5, CHRM2, TMEM216, OR8U3, APOM, NSFL1C, ALK, GRM5, GBA2, LAMP3, CYP2C8, HDAC6, NR0B2, NR1D1, IL22, TRPM3, HTR2C, HERC2, FBXO7, REL, PER2, MAP2, SERPINF2, RBBP7, ADRA2B, HMGA1, TGFBR3, ADD3, DR1, CYP24A1, KCNE1, FBXW7, KAT8, IQCB1, CYP51A1, CLASP1, BAG6, TIMELESS, CDKN2B, FIBP, ADAMTS4, CEL, GHSR, DAG1, ARHGEF1, MASP2, VPS13C, UBE2D2, GJC1, TTC21B, FGF19, CD2, AIFM1, LOC110806262, RPS6KA1, RPL13A, PDIA2, SGPL1, LITAF, INSL3, MIR24-1, CEACAM5, DNAH5, EDN2, TTC7A, PCBP4, CCR4, PMP22, ADARB1, MYH6, PPFIA1, CHKA, TBL2, PCSK7, DYNC2I2, RTEL1, CPT1A, TTPA, GHRH, TSPAN7, MAFB, AIPL1, PNPLA2, MYO5B, CFP, SCAP, PCIF1, FHIT, EPHB2, EBF1, NRIP1, SGK1, PRPH2, BMP7, XRCC3, FBN2, NOX4, CCT2, TNFRSF4, COPA, HSP90B1, SLC25A22, DYNC2I1, CDC7, MIR126, ROCK1, AXL, GMNN, CD1A, ESRRA, FHL2, PIGR, SERPINA6, ATP8B1, KLF5, SLC7A9, ADRA1A, SGSH, GNL3, CSPP1, ZBTB16, TAP2, PROX1, MAPKAP1, RAB23, IFT46, NPHP3, CSNK1A1, EDC4, ASAH2, ANG, SPRY2, MIR122, PCM1, USP36, NCOA2, CYSLTR2, KCNJ12, SLC7A11, IFT56, MBTPS1, HRH2, ALOX5AP, DENR, MASP1, PDE4A, ADH7, TENT2, BUD13, LSM2, NMNAT1, AGO1, CRHR1, HIRA, DSG2, ECE1, TIMP3, NFATC2, CEP192, NUP133, URB2, MMP12, NSUN2, HTR6, EHD1, FAM161A, SSTR3, KIFC3, CSF2RB, LZTR1, SEMA3F, SNORD44, GPAM, PPP3CA, PPIG, CFD, ATF6, TNXA, IL12RB1, CDH23, F11, OSBP, FGF21, HYOU1, ATP1B4, ETV6, ATP1A1, UNC119, GCDH, ECHS1, NPY2R, INPP5E, IFNAR2, CAPN3, UGT1A10, ROCK2, PGF, MRM1, NEUROD1, TPMT, STARD3, CSDE1, EVC, ATG7, CAPN10, AVPR2, JMJD1C, GHRHR, PKN1, DISC2, RPL7A, SLC25A12, EXOC5, IFT57, HNF1B, VCPIP1, BABAM2, NECTIN3, TNFRSF11A, ILF3, KIAA0586, CYP11B2,	

	LHX1, FAM13A, MED12L, TXNRD2, SYN3, RAB3IP, HDAC8, HSD17B4, ARL6IP6, PTGDS, LCT, GSTM3, LRP6, MYBBP1A, TULP1, TNFSF14, ATP1A2, DCDC2, ACAA2, CAV3, NPHS2, CD48, GPX4, GRIK2, CYP3A5, TBXAS1, ROM1, EIF4EBP1, SLPI, PRKACB, HAVCR2, CAPN2, ATF1, MYLK, APLN, CCL20, GCLC, EBP, MIP, CYSLTR1, GAB1, SCP2, TRAF3IP1, PYY, FDFT1, UGP2, UTRN, INF2, ADRA2C, PAX4, CILK1, LOC126805877, PDE6D, EN1, FABP12, IFT80, HTR1B, CX3CR1, CFI, MYZAP, MCHR1, CNTN6, CEP131, MIR486-1, ADRA1D, MAT1A, OSBPL8, PCSK5, GAB2, CHKB-CPT1B, RHBG, SLC8A1, STX3, CTF1, SEPTIN2, CHIA, SIM1, PCSK2, B9D1, TPH2, CAMK4, PRMT3, TGFBI, FBP1, ZYX, KCNA1, USH1C, TMEM231, MARS1, HSCB, SND1, NFAT5, MAP3K3, RARRES2, AHSG, NISCH, TIMD4, RAB11B, COMP, CHI3L1, TRAPPC3, FHOD1, SOD3, KCNA5, NRF1, FLG, TNXB, CD74, TRPM8, ACP3, PROCR, FAF1, TMEM175, PNPLA3, ALOX12, AGL, SLC2A10, WEE1, NLRC5, ZDHHC24, IFT20, P2RX7, SERPIND1, NFATC1, RAD23A, ADCY3, AGTR2, VEGFB, TRAF1, TNFRSF9, OIP5-AS1, KIF5A, GPNMB, RPGRIP1, ACLY, GCGR, AHI1, MST1R, MYBPC1, KIF13B, TMEM138, MTHFD1, P2RY1, GK, MPV17, BAD, PCCB, PKD1L1, PNN, POLR3GP2, CALM3, GRK3, BDKRB1, MYL2, GULP1, NCF4, FADS3, FLII, IFNGR1, IFNA2, UBE2G2, CD5L, CEP41, ANKRD28, ADH5, F2RL3, CRYBG3, NCOA6, ELP1, CCND3, MTRR, RNU6-1, PDE4D, MIR9-1, PSRC1, CC2D2A, CADM1, NR5A2, ACAD8, HLA-DMA, MIR31HG, CISH, RBM6, LMO1, TSPOAP1, TUT4, TCP1, OSBPL1A, ZMYND8, AVPR1A, EIF2AK3, ZIC2, CAST, MIR484, ALDH1B1, SLC7A6, RFX3, PDE6A, ARHGEF11, ARHGAP44, PNPLA5, SNORD63, CIMAP3, PSPH, RDH12, PERP, ADCY5, RILP, CCP110, DUSP2, S1PR1, SYN2, ALAS1, SRI, FGG, PDK4, LCN2, PTGER3, ZNHIT3, GJB4, DNAJC13, TCTN1, ATP2B1, KDSR, FOSL1, BCL2L14, FER, TBC1D32, SERPINA12, FAS-AS1, NEB, LINC00261, RGS4, FITM2, VEGFC, STX8, CEBPD, ARHGEF12, ABCD3, HAP1, TREM2, FOXP1, LRPAP1, RAB28, TCTN2, EDF1, IL13RA1, ASCC3, DOCK6, HCAR2, OTX2, SLC2A2, MIR144, TEC, FABP1, SHMT2, CSNK1E, DNAH17, TPH1, GGCX, OLR1, CMIP, PPIL2, COX10, POU2F2, IL12RB2, GALK1, IGF2BP3, MYO9A, ODF2, PRMT7, DPP3, UGT1A6, LRP8, PLCB4, AQP3, PTGER2, SCD, ADIPOR1, ADAM10, SLC11A2, POU2AF1, GP5, CAV2, AQP9, TRAP1, TUB, GPR161, GNMT, PROP1, TFR2, PLCB3, INPPL1, FNDC5, RING1, CCR1, SSTR2, RAPGEF1, SLC6A17, MIR143, HLA-DPA1, NFKB2, UGT1A7, ARL3, SLC7A8, DLC1, KLKB1, GRB14, CELSR2, SLC25A10, UGT1A9, MAPK8IP3, GNG2, MMP8, SLC19A2, CLRN1, TFDP2, TAGLN, DGAT1, NSMCE2, CNR2, IL16, FCER1G, RNGTT, SLC22A1, ALDH9A1, TANK, PSD3, COL5A2, GABPA, SOX6, CHRM1, CERKL, SLC22A12, DLX5, EXOC3L2, ALOX15, IL9, RSPO3, TBL1X, TBC1D4, CLASRP, AMBP, CIB1, CIR1, EBF2, SLC29A1, GPRC6A, MAPK13, RBP1, F8A1, CELSR1, CNP, ATIC, DXO, RP1, SIVA1, CD22, HDGF, CDH13, KANK2, MEF2D, TRPV5, EFHC2, PTGES, NUDT6, CPB2, SERPINA5, GSS, TOP3B, MIR31, RABL2A, PNMT, TAF11, WNT2, CALM2, SPATA7, GABRA2, IFT25, TNNT3, CA9, IL11RA, PPRC1, ICAM3, MESD, RGS2, MDM4, ROS1, SERPINA4, ANP32A, LMCD1, SLC2A9, IL1RL1, CTSK, SUFU, C7, MGLL, DMPK, DLK1, NDUFS2, ARL4D, COBLL1, ARMC9, GBA3, ABO, PKMYT1, KIF24, BLOC1S4, NAA10, CHRNA5, CCL19, MAML1, TFPT, TK1, NFKBIB, UVRAG, L3MBTL1, DGAT2, KLF14, HLA-DMB, ATP1B1, CFHR1, LOC129931597, FOXC2, MIR24-2, DUS2, CD3E, CPSF4, FDPS, DCD, TRMU, PDE6B, MTX1, CLUAP1, RELB, PDE3B, TBX3, KLB,	

	ADIPOR2, BCL7B, LOC129935068, IGFBP6, WNT1, IFNE, CNGB1, PRKRA, MMP11, MIR33B, OCA2, CLUH, ANXA4, CASD1, CYP11B1, CEP164, LCA5, PTPRM, LOC129998833, CDIPT, ABCC9, PTGDR, SCNN1A, HNRNPUL1, MAP4K2, SENP3, LILRA3, KCNQ3, CFAP410, WNK3, BAG3, MED22, RABIF, DEFA1, ADK, SUGP1, LOC106560211, HPX, DNAI1, RREB1, C5AR2, MADD, NT5C3A, CEP250, ATAD3B, RP1L1, CENPS, ABL2, MEIS1, SNTA1, LLGL1, ITGB5, HAVCR1, HDAC5, THBS2, AGPAT1, ATP6V0A2, LOC126806173, TTBK2, PEMT, MSBP1, GPR55, AZGP1, RARG, CYP4A11, FREM1, HCAR1, C1QA, LOC126806252, ZNF462, CYP4B1, SCAF1, ABHD5, SEMA3C, LUC7L, CALCR, C2CD3, ASGR1, ARF3, CHCHD10, PAPPA-AS1, CCL27, TADA3, ESS2, TRAPPC11, PSMB4, UTS2, HCN4, CHGB, MICAL1, NCOA4, PER3, ST8SIA4, RGS9, GRK5, DLG2, PBRM1, CACNG2-DT, GCLM, PTGFR, MIR136, SLC16A3, BAG1, CYP46A1, GIPC1, KCNJ1, PAG1, UBE3C, GAS7, CEP83, RAB29, MIR30C1, PRKD2, CDK5R1, STK19, TIMM8A, PSMA6, SOCS2, PWAR4, SDC4, BCL9, EFCAB7, CLTA, MTR, A2M, HSPA1L, IRS4, C9, NOX5, NEK8, IL5RA, TCF7, HDLBP, NFIA, CHRNA1, DPH3, RAVER1, PTPRN, ADORA3, PTGR1, MMP25, CD79B, SPATA31H1, GRHL3, SLCO4C1, TBL1Y, HSD3B7, CCDC28B, DEPTOR, MIR1260A, KCNMB1, MYBPC2, MAP7, NCR3, ALCAM, KLF3, WARS1, USP53, GABPB1, CAMK1, NFATC3, SH2B3, EFR3B, PPP1R1B, LGALS2, RILPL1, VPS39, IGF2BP2, ACKR1, MAP2K5, AMPD3, RFX2, CNTLN, CYP4F2, PCARE, BCL2L2, FLRT1, MCAM, DLGAP1, ADORA2B, BHLHE40, HPGDS, LGR5, GIT2, SCO2, MAK, EFHC1, AKR1C4, ITPR3, IL10RA, GSTM2, OSBP2, ITGB6, HPR, GPSM3, SLC46A1, BBOX1, RENBP, MPDZ, LOC126805794, POSTN, MYO3B, NPDC1, MIR6886, NFKBIL1, SLC25A37, CTH, CNGA1, TULP3, MIR216A, ZFYVE9, RAP1GDS1, HMGA2, SIN3B, TPM2, ANKRD27, ACSL1, VAMP8, MYO1H, GYS1, HSH2D, IFT88, THBS3, PCK1, PTX3, SFRP4, LAMC2, C1QC, MAFA, ANKRD13D, PLCL1, BIK, MVD, KCNC1, LOC157273, UGT1A8, B9D2, CTSF, GSTO1, LTBP4, ERG28, GBF1, HMGCS1, ME1, BAIAP2L1, MIR148A, RAB26, CAPN5, PKP3, F2RL2, RAB3GAP1, CDKAL1, MTNR1A, MIR4713HG, MPIG6B, MBTPS2, NFIB, DMP1, SETBP1, CCKAR, LILRB1, MGP, PINX1, CXCL16, TNFSF13, FBF1, LINC01094, MSI2, SIX5, MYL3, HMGCS2, NTNG2, IFNGR2, GORASP1, DUOX2, NOP9, IFT70B, IFT22, MARCHF9, FOXJ1, CEP97, ASB4, NLRP12, SCNN1G, GLMN, FNDC3A, NR1D2, CXCR1, SCARNA17, AOC1, CHRD, TOP1MT, MACF1, CD72, NFATC4, PCMT1, SDHD, AOX1, FUT3, EPHA1, OGA, RABAC1, SLC39A8, SLC4A5, IQCE, CROCC, SLC25A2, NPB, MIR1207, LOC106627982, INSIG1, TIE1, KLK1, UGT1A3, RGS7, TPSAB1, HHEX, INPP5D, LMAN1, OGN, DCLK2, CPEB4, ADAM33, UGT1A4, PLCH1, CREBRF, CLCNKB, PSMB9, FPR3, MICA, NOS1AP, ATP6AP1, COL11A1, RPH3A, KCNK4, LSS, BRAP, PTAFR, NPSR1, ARHGAP45, C2, NPY1R, VARS1, FOLR2, GPATCH4, KDM2B, DGKB, PGS1, EIF2B5, ANO1, NRG3, MAP3K6, DUSP4, CRY2, PELO, CYP2J2, PDE6C, LSP1, CH25H, TMEM107, CEP89, KRTCAP3, AKAP10, ADAMTS9, MSRA, KRR1, DNAJB11, GTF3C5, HSF4, FES, IQGAP2, BCL3, SLC14A2, GPR50, ENGASE, SLC28A3, GNA14, NLGN4X, MAPKAPK3, MTHFD1L, SELENOP, AKR1B10, PPP3CB, PSKH1, IL1RAP, COL11A2, ALDH1L1, ZFP90, OMP, KCNK2, ATP5IF1, PLLP, NXNL1, SPMIP6, RNU105C, LOC126806306, LOC116158507, LOC126863139, ZNF2, AFF1, PTPRO, HIVEP3, STAB1, MYO1D, CMTM6, SHPK, SIDT2, GRIN3A, AKT3, SQLE, TRHDE, NMT2, PKNOX1, CENPT, OFCC1, CYP7B1, ITPR2,	

	ZBTB20, BAG4, MOGAT2, NYAP2, SLC30A8, SLC4A2, IL17RB, EDN3, SLAMF6, KCNE3, TNNI2, CARD10, PHC1, ADGRL3, HABP2, APC2, ADGRE5, CALU, MCFD2, LYRM4, IL10RB, GBE1, ITLN1, SLC27A1, PTGDR2, IL23R, MIR196A2, NELL1, SGCD, SLC39A6, PIGV, FBXL8, CDC123, BTN2A1, ABCD2, IRX4, CDK5RAP2, GRK6, LYZ, CERS2, SLC27A4, DPYSL5, ID4, TMEM70, EIF2B1, MIR485, CARD16, SURF4, CSRP3, VCX, CLTB, INTS11, DPP6, PPP3R1, AMPD1, MMP24, LINC-PINT, SYN1, MTHFSD, LPAR1, LTB, TREM1, SRGAP2, SCAND1, ABCC3, PLCB2, MIR550A3, SLC30A1, THOC6, ENTPD6, SOX17, SNTB2, MYO16, TCN1, INTS10, ST3GAL4, MMP10, DTNB, RAMP2, HCRTR2, TNNT1, USP24, TNFAIP2, FFAR1, KCNK9, ZNF644, TNIK, PTGER1, AMY1A, BORCS8, SOCS6, CABIN1, IRAK2, STARD13, GPATCH8, SPATS2L, C7orf50, PDE4B, TRIOBP, TRERF1, LOC108491825, ERGIC3, NDUFV2, PIK3C2B, REEP5, CACTIN, MIR149, SIK3, ACVR2A, PLA2G10, SPTY2D1, TUBA8, MEF2B, TRPC1, NDN, MAT2A, DUSP10, RPIA, NCAPH2, CCL28, BAHD1, MSL2, SLC45A2, SEMA5A, USP9Y, VPS11, IGF2-AS, GRM3, UPB1, ARAP1, SLC22A2, KCNE2, PAN2, CCDC86, ACOX1, FOLR1, C8A, IL1R2, MIR99AHG, ABCA10, CYYR1, MATCAP1, PTTG1IP, FABP3, MACO1, EPX, PROK1, DOCK2, CLPTM1, SCAF4, CES2, PTK6, ERAP1, GLIS1, CEP57, DDAH2, LRP2, GLIPR1, CEMIP, UGT1A5, IL17F, GPR179, SULF1, FAM50A, PIKFYVE, LPIN1, MCM8, SOSTDC1, PLA2G5, BAG5, LAMA5, SLC34A2, MTFP1, HBS1L, PTPRD, CARTPT, SV2B, ASIP, INSRR, CTSH, ZNF407, AOC3, PTGER4, LILRA5, FBXO46, NIFK-AS1, LOC110596866	

Supplementary Table 12.Baseline characteristics of MFT samples

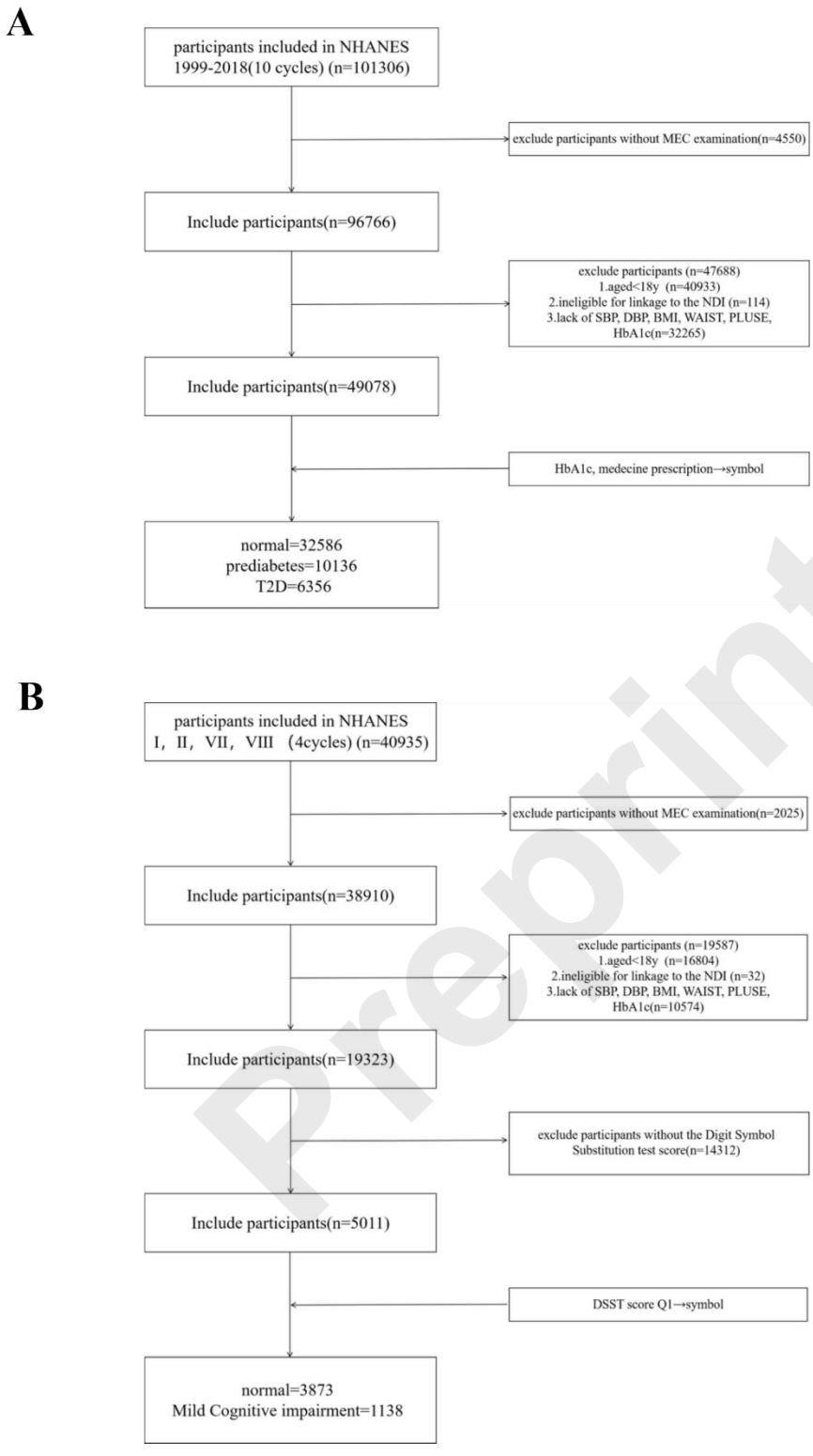
	Ctrl	T2D	*P*
	n=23	n=17	
Age	37 [32, 45]	40 [35, 52.5]	0.2654
Weight (kg)	78.5 [73.3, 88.6]	86.1 [72.55, 98.8]	0.4685
BMI (kg/m^2)	28.83 [26.25, 32.29]	31.05 [27.47, 38.46]	0.2108
FBG (mmol/L)	4.8 [4.22, 5.11]	5.44 [4.88, 6.125]	0.0042
Total cholesterol (mmol/L)	4.53 [4.09, 5.865]	5.155 [4.88, 5.713]	0.1447
Triglyceride (mmol/L)	1.19 [0.92, 1.885]	1.795 [1.373, 2.705]	0.0352
LDL-C (mmol/L)	3.01 [2.58, 3.965]	3.57 [3.123, 4.270]	0.249
HDL-C (mmol/L)	1.09 [0.9225, 1.268]	0.95 [0.885, 1.11]	0.1208
HbA1c (%)	5.15 [4.85, 5.3]	5.9 [5.525, 6.325]	＜0.0001
β-HB (mmol/L)	0.3 [0.18, 0.75]	0.12 [0.85, 0.35]	0.0222

Supplementary Table 13. Degs in transcriptomic analysis of MFT response

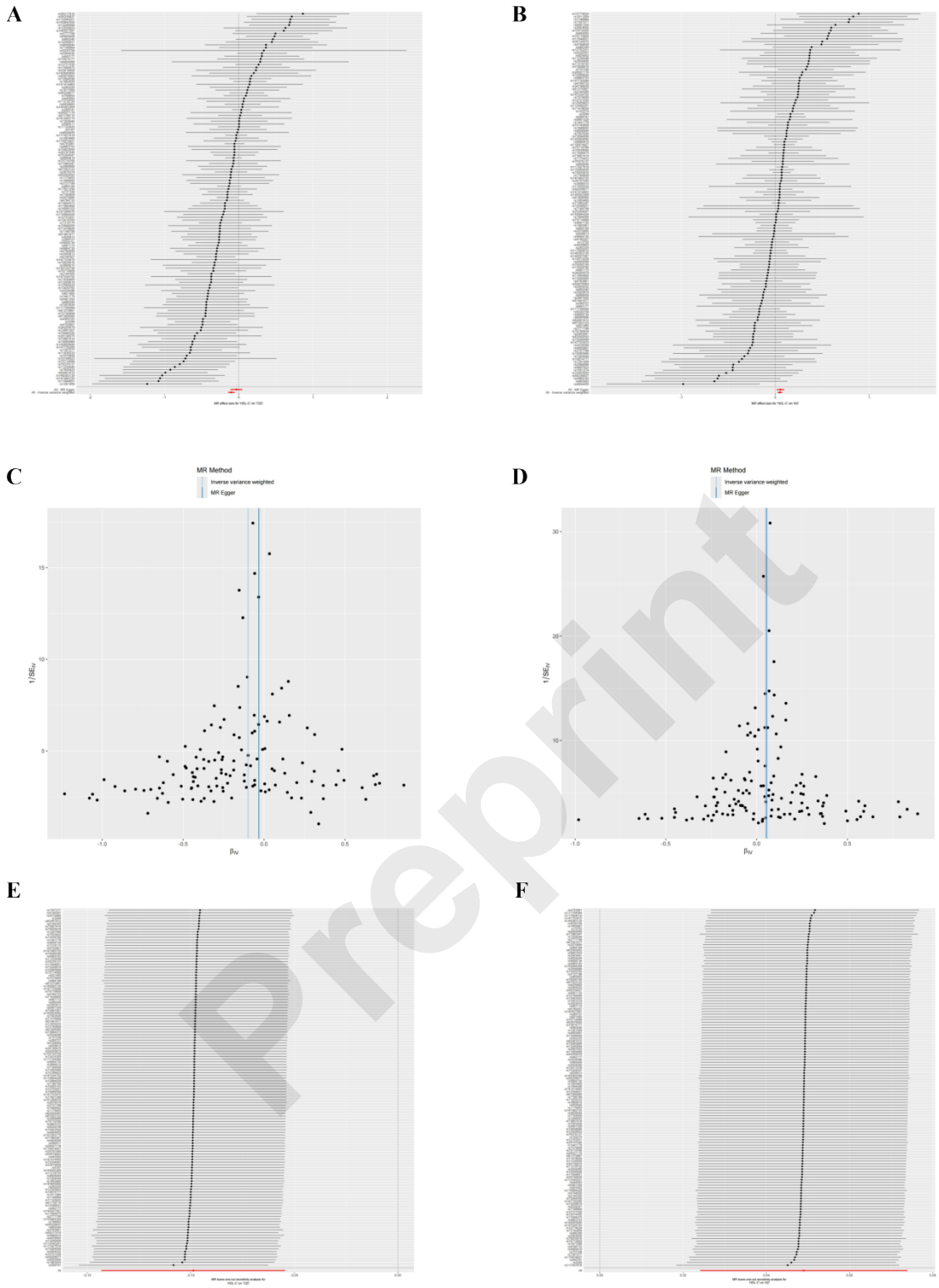
	Gene	Number
Pre-post up-regulated Degs	LINC02908, GK5, LINC02175, SLC4A4, SYT11, TMEM44, DTX3, KATNAL1, STX16-NPEPL1, PRTFDC1, ARHGEF40, HDAC9, MYL5, NOXA1, NEIL1, KLRK1-AS1, SPATA6, JHY, ANKAR, SLC11A1, DENND6B, CCDC71, PARL, IL1R2, PTGDS, ABCC3, FDXR, INSR, CCDC136, ERCC1, SPINT1, CYP2S1, C1QTNF3, GGACT, THTPA, MRPS28, PLXNA2, ADA, CD9, EPN2, PLB1, SEPTIN10, KRBA1, RRAS, NDUFAF8, NPEPL1, ZNF528-AS1, CSF1R, DHCR24, TRIB3, LINC02481, C1orf54, SMYD3, HCST, DHPS, CACNA1I, CCDC170, MEF2C-AS1, CDH23, KAZN, TNNT1, EIF4A1P4, ADAP2, IGFLR1, SNX21, P2RX1, FSTL1, SALL2, TRPM6, PLCH2, PLXNB1, MELTF, BAIAP3, GPR162, LINC00943, RPL3P7, RASGEF1A, H2BC15, STON1, KCNMB1, MSC-AS1, MYRF, ABI3, SPATA20, HOPX, WHRN, NLRP6, MAP4K1, GNRHR2, PIRAT1, RNF32, IFT140, TFAP2E-AS1, CATSPER2, SYNGR1, ARHGAP6, NAV1, COL6A2, PTPRS, ZFAS1, CUEDC1, PGM5P2, ST8SIA6, ZBTB16, HOXB-AS1, RIMS3, KRT73-AS1, TAGLN, ATP8B3, TRIM7, RBPMS, PYROXD2, GP1BA, SIL1, RTEL1-TNFRSF6B, STARD4-AS1, SPACA6, DRAIC, LYRM9, SSH3, MIRLET7BHG, DOCK6, ICA1, SOX4, LINC02915, PLD4, LOC105375754, CCDC9B, CPT1A, CDC42BPA, ZNF321P, TPST1, PDZD4, CHI3L1, ACP2, ASIC3, M1AP, DGKG, LOC124902027, FAM228B, ADGRD1, CLEC10A, AJM1, FKBP5, LINC00639, GPRASP2, TPH1, LRRC51, NT5DC2, CACNA1H, LINC02289, PPP2R2B, COL9A2, MERTK, ARAP1-AS2, THNSL2, PTGIR, KRTCAP3, H3C10, MIR186, GIPR, TMEM147-AS1, CRYBG2, ZNF365, EPM2A-DT, TSPOAP1, PIGL, FADS2, RASL11A, LOC107985216, ARK2C, FKBP14, RALY-AS1, SASH1, PAQR7, GNGT2, WBP2NL, ST14, UBE2FP3, HSPA7, S100Z, LINC02910, H1-0, ARVCF, APOBEC3H, KLHDC8B, OTX1, ZNF425, BAIAP2, SCN1B, KLRF1, MIR3682, SELENOM, FADS1, DNM1P46, FLT3, TANC1, EBF4, FGFRL1, CEBPD, ST8SIA6-AS1, ANKRD6, SCN8A, TFAP2E, OCM, DICER1-AS1, LINC00173, MYO7A, DTHD1, RHOC, ELOVL6, KLRD1, SGSM3, PPFIA4, FAM66C, GPR199P, PID1, SPON2, PDGFC, WNT1, NMUR1, PZP, NFIA, SPATA31H1, LOC102724104, QPRT, XPOTP1, RGS9, WASF3, LINC01750, LINC00299, ZNF219, GLB1L2, CLDN20, GFOD1, PRELID2, LINC02324, GRK4, TNNC2, GRIN2C, B3GAT1, LOC127814295, RYR1, DUSP1, SPTSSB, TENM1, CHPF, KLF9, RPGRIP1, LOC100506274, PRKCZ-AS1, CACNB1, MMP9, C3orf20, PRRT2, EFNA5, FAM131B, BMS1P1, SLC5A9, CIB2, SMIM10L2A, RPS20P6, NID1, C10orf105, SORCS2, LASP1NB, TSC22D3, LINC01819, ECT2L, RPL31P43, DRAXIN, LOC105376995, CKB, LINC02610, GCNT7, IL1RL1, CEBPA-DT, RAPH1, CARD9, SIGLEC17P, APCDD1, TRGV1, AMOTL1, GUSBP9, DGKK, TMPRSS13, SLC9A5, GASK1A, CACNG6, UGGT2, SPAG8, VENTX, LINC01841, ZNF628, DNM1, TMEM255A, CD160, RAB4A-AS1, ADGRG6, VWF, MYCBPAP, SRRM2-AS1, KCNC3, CCT6B, UPK3A, TRIM17, TRIM74, CDHR1, FAM81B, CC2D2B, CRIP3, CFAP45, ECHDC3, LOC107985211, RPS3AP18, MACROD1, LOC105370174, FTH1P22, MRAS, PDGFRB, CHCHD6, SCNN1A, RPS15AP27, SH3RF1, LINC01191, PDE6G, ZFPM1, LOC105369656, RN7SL834P, C6orf226, FPGT-TNNI3K, SEZ6L, AXL, SEPTIN7P8, LCA5L, RAG1, KNDC1, ADGRA2, ADGRB2, MIR646HG, MCF2L2, PTGDR, STRIP2, PDK4, CRABP2, FAM114A1, DPEP3, LINC01451, GCHFR, TSHR, PXN-AS1, ERMN, MUC1, LDB2, GUCY2C, TNR, PROX2, GPR153, NEURL1, LRP5, ANP32AP1,	447

	LOC644169, TP53TG5, VPS28, ITGAD, LINC01088, SAP30-DT, ASPDH, TRIM73, SCAMP5, AQP10, ZNF469, OLFM1, SSPOP, SPRED1, HIC1, RPS10P1, RCAN2, MAGI2, RNY1, FLJ40194, CNTF, SCARNA9, IRS2, MYZAP, TM4SF19-AS1, POLR2J4, RTEL1, SCNN1D, NECAB2, KCNB1, COPZ2, NHERF4, LINC00908, KCNE1, GLI3, PEG13, EFR3B, FEZ1, LINC02288, H2AC8, TMIGD3, YY2, LRRC36, GRID2IP, SLC25A27, LOXL4, NHERF2, LOC101929719, LINC02937, SHE, AURKC, DDR2, LPL, PAOX, CNNM3-DT, PER1, LYNX1, CD1B, EPS8, SLC35D3, GFRA2, LOC101929538, IL6ST-DT, RPL17P24, NEURL1B, F12, AIDAP2, LOC124902477, DDIT4, LOC124900217, TRDJ2, ITGB4, RET, TACSTD2, UICLM, ARHGAP29, SFN, TMEM119, MIR4420, PPP1R17, GPER1, RPL7AP82, CROCC2, FOSB, SLED1, LYPD2	
Pre-post down-regulated Degs	ID3, IL31RA, EMID1, ALAS2, BTBD10P1, TSPAN6, KLC3, PDCD1LG2, LOC100996318, CXCR5, B3GALT2, C4BPA, RN7SL3, SENP8, ADRB1, ANKRD31, MRPL46, SLC6A9, LINC02217, TRAV30, H4C14, ASTN2, RPL21P98, EPB42, RN7SKP70, CICP27, UBE2C, ABCA13, CEACAM6, GCAT, FZD5, MCOLN3, CCR9, SLC4A1, SELENBP1, CISH, SMARCA1, C22orf23, BASP1-AS1, CD274, KRT1, PRSS35, ACSM1, PEX12, ALKBH3-AS1, AHSP, NOG, TRAV36DV7, IL1B, TRAV35, HACD1, DLGAP1-AS3, MRC2, NEBL, YPEL4, FAM83D, ASPM, HBD, KAT7P1, LIPH, GPR18, NPAS2, PLVAP, HBG1, OLFM4, KCNJ2, LSMEM1, TTK, LINC00216, HBB, MYORG, IGKJ5, TRBV7-6, SLC7A8, RUNDC3A, KNL1, TRAV39, IGKJ4, DUXAP1, PRAG1, ZBTB3, LRRC46, HBM, RIMBP3, SLC25A39, RWDD3, BBS12, CKAP2L, FAM124B, ADTRP, ZGLP1, ITGA9, VWCE, ENAH, CCR8, HBA2, IGHV2-70, RPL4P1, RFPL2, ADM, ANKRD36BP2, LYRM4-AS1, TNS1, OSBP2, SNCA, PSPN, SLC16A1, RBM11, ZNF366, HBQ1, EFCAB10-AS1, TRAV10, SLC6A8, ODAD4, GPR146, RAD54B, SMG8, KLF1, MATR3, SPATA41, SUCLG2-DT, CA6, AQP1, ADGRF3, HBA1, GPR15, KTN1-AS1, MOCS3, TRAV2, SERTAD1, TRAV22, THBS4-AS1, PLEK2, ZNF667, KCNIP2, CDK13-DT, GATA1, CCR7, LOC254896, FBXO5, THOC3, UBXN6, AK5, ABCG2, RAD51AP1, DSC1, ECT2, PDZK1IP1, RBM7, SLC38A5, DMTN, MYL4, USP31, MLLT3, NUAK2, PDE4B, PROCA1, ITGA10, DACT1, MSANTD2-AS1, ARL2, MRPL44, GMPR, SMIM24, TIFA, ZNF574, KREMEN1, CMTR2, IL23A, E2F2, HSPH1, TESC, LRP2BP, PRRG4, CLP1, LCN2, ZNF284, RAB20, AVIL, PIM2, LYL1, TRBV5-4, BOLA1, CD24, ZNF626, GRB10, CENPN, EXT1, ITGA3, A1BG-AS1, ZBTB18, LRRN3, DNA2, OVCH1-AS1, GUK1, RASGRP3, EPHB4, DDIAS, PLPP1, RPUSD2, ZSWIM1, RGCC, ZC3H11C, TCN1, TENT5C, ST6GALNAC4, CKS2, TAS1R3, AXIN2, PRICKLE3, GYPC, SOD2, GMNN, CD40, ASCC2, NDUFAF4, DPM2, TRMT10C, PUSL1, CPT1B, EMC3, HPSE, EPB41L5, PI3, PFKFB3, ALKBH2, MYC, KBTBD8, TBCK, PPA1, BIRC3, LRRC8B, MAGI3, NFKBIE, ZNF92, MINPP1, FKBP8, ZNF408, WWC2, ZNF124, BAG1, MRPS18A, DNAJA1, CYB5A, ARHGEF19, TRAV13-1	246

Supplementary Figure

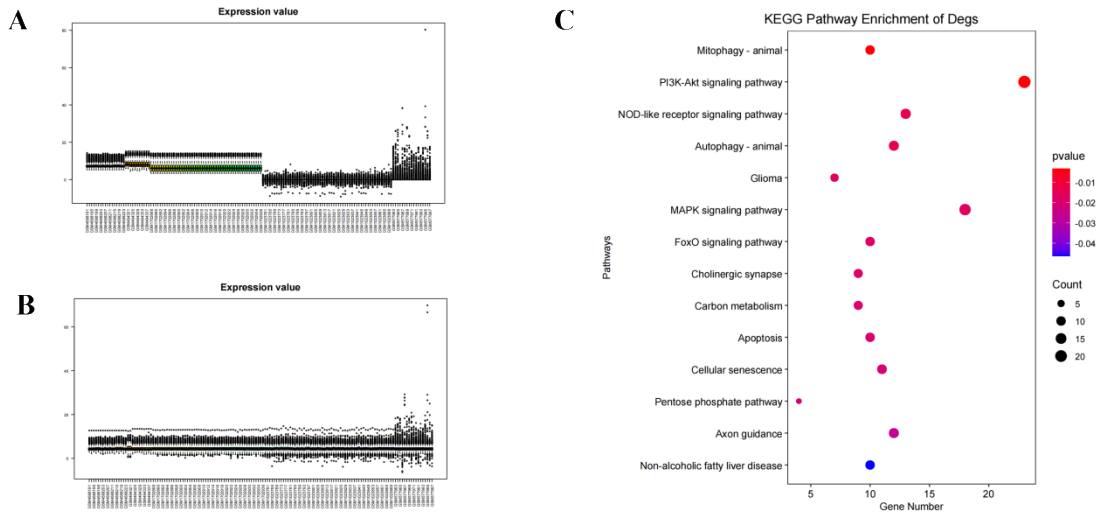


Supplementary Figure 1. Flow chart .The selection of eligible participants in the NHANES. A. T2D; B.MCI

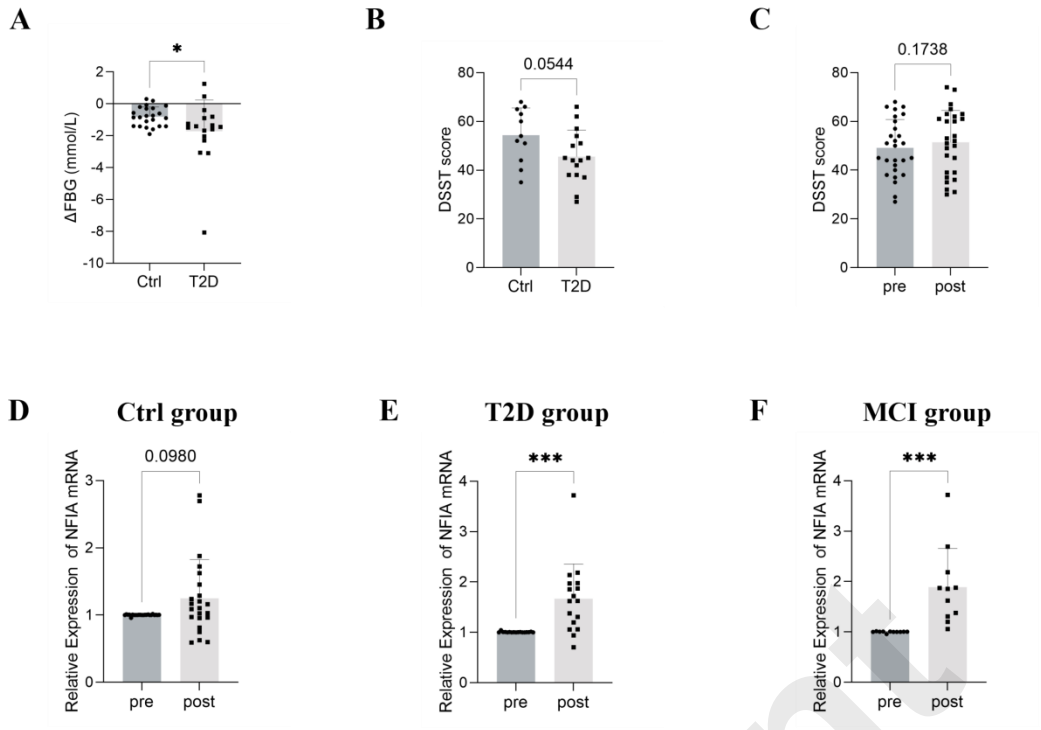


Supplementary Figure 2. A-B. Forest plots for MR analyses; C-D. Funnel plots for MR analyses; E-F. Plots of "leave-one-out" analyses for MR analyses.

Across all figures, Exposure: HDL-C. Outcomes:T2D in Fig. A, C, E; MCI in Fig. B, D, F.

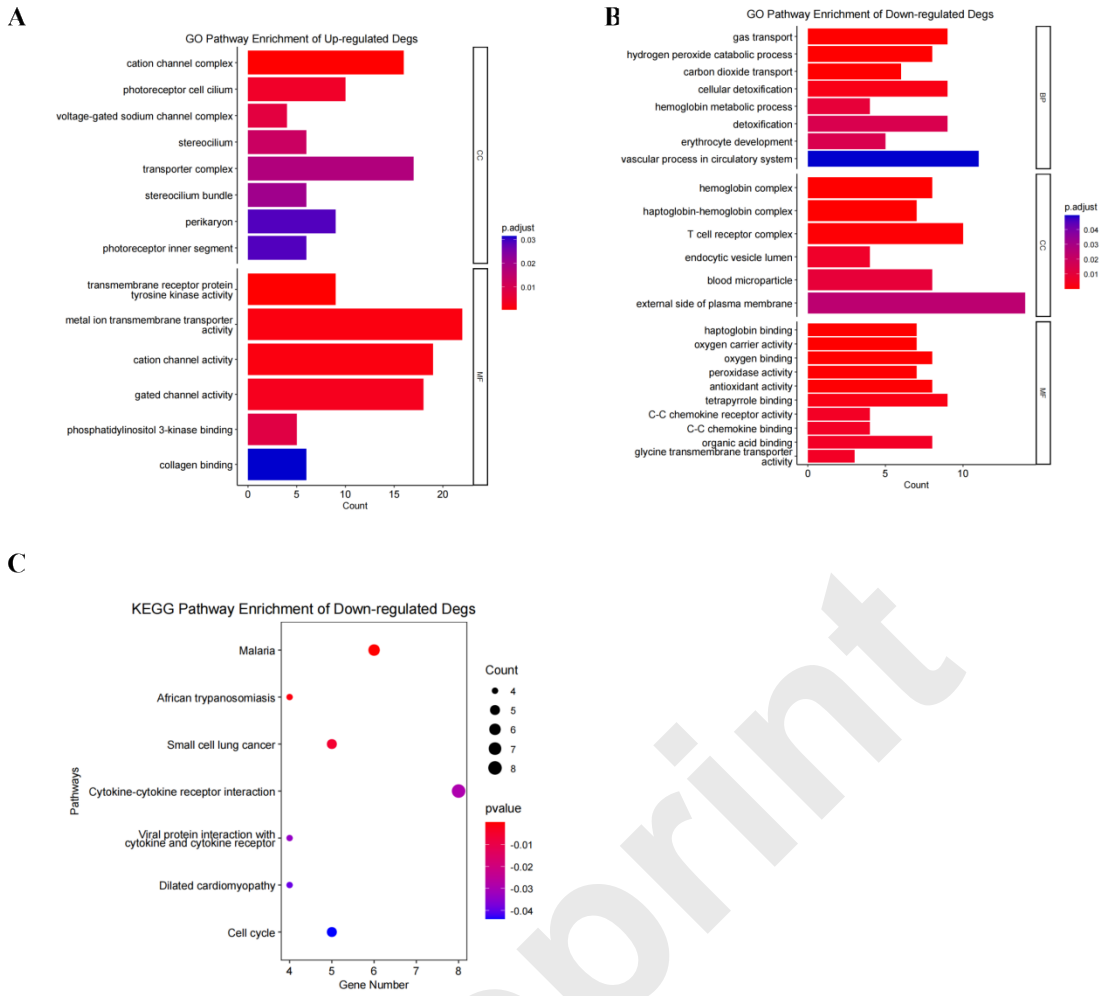


Supplementary Figure 3. A-B. Removal of batch effects in different datasets; C.KEGG enrichment of Degs;

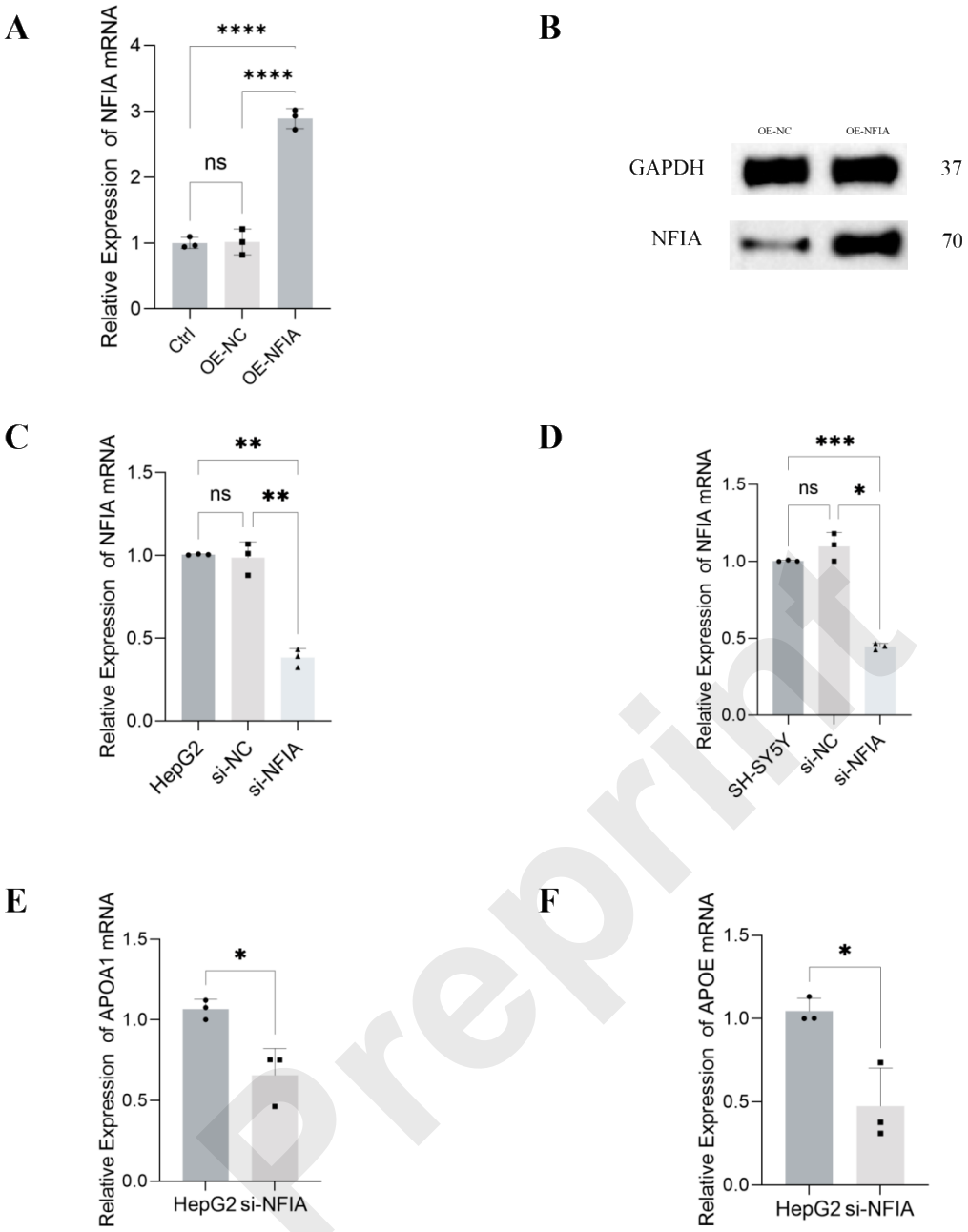


Supplementary Figure 4. Analysis of relevant indicators before and after Modified Fasting Therapy. A. Changes in FBG after Modified Fasting Therapy. Ctrl: n=23 , T2D: n=17 ; B. DSST scores for T2D and Ctrl groups at baseline, Ctrl: n=11, T2D: n=16; C. DSST score before and after Modified Fasting Therapy, n=27; D-F. Expression of NFIA in peripheral blood among different groups, D. Ctrl: n=23, E. T2D: n=17, F. MCI: n=11

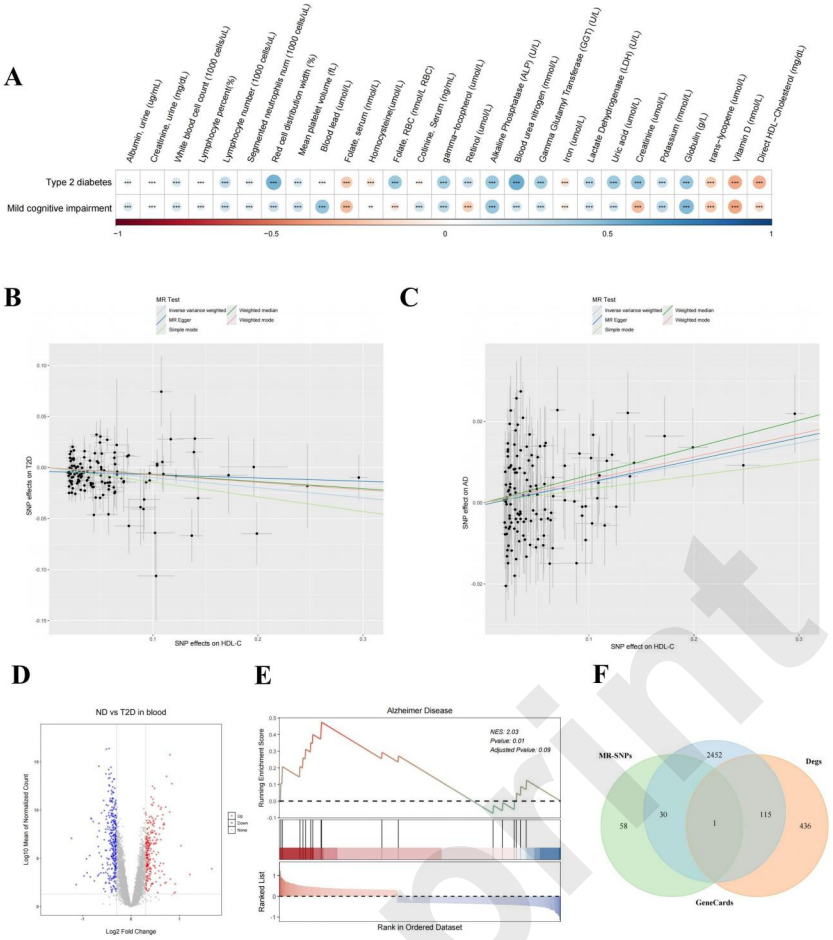
All plots are shown as Mean ± SD. *p<0.05,**p<0.01,***p<0.001,****p<0.0001

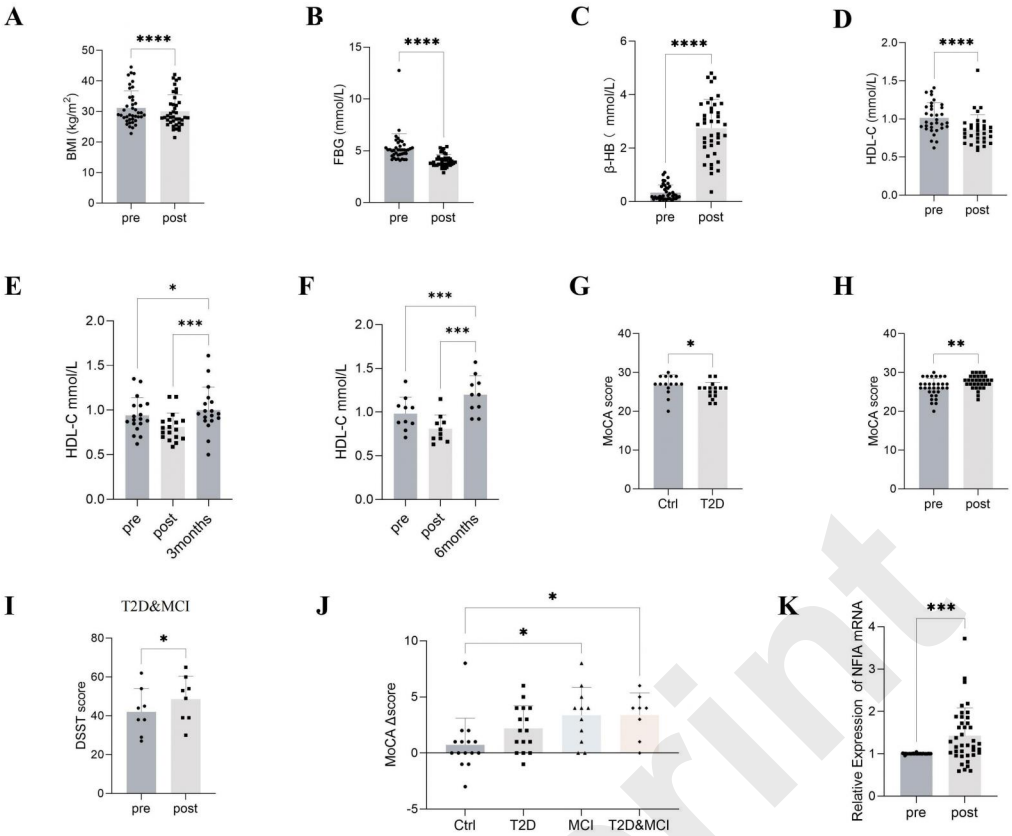


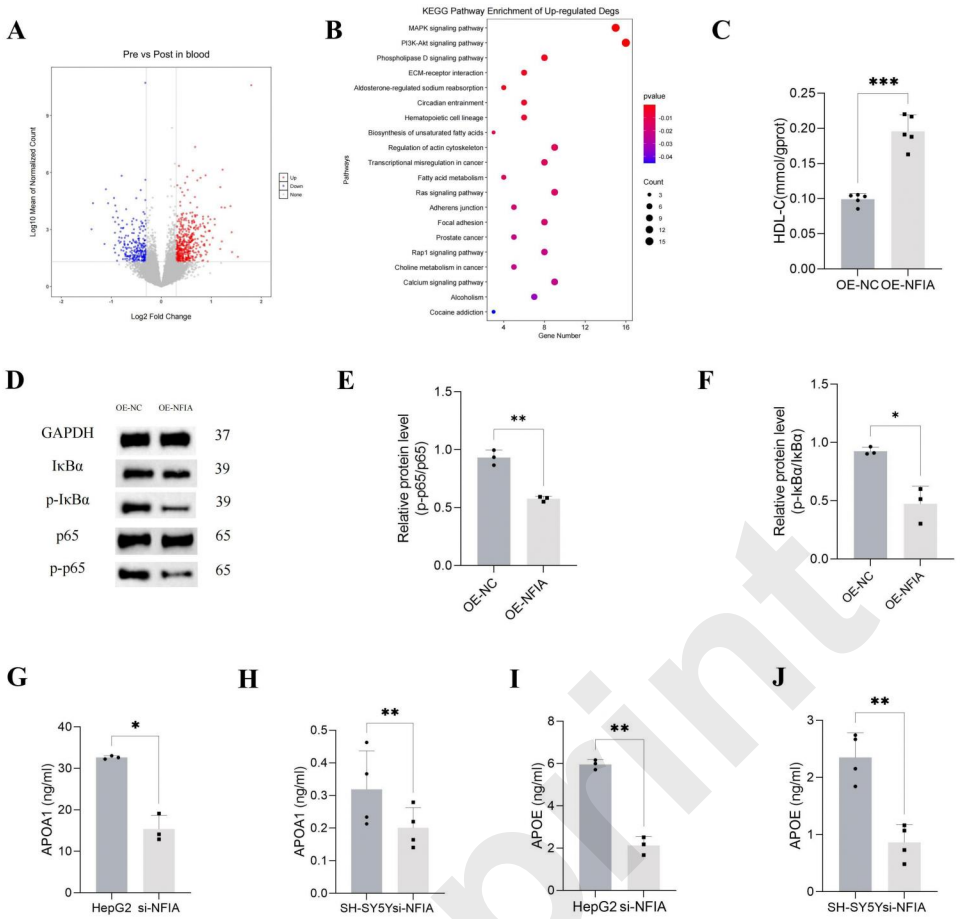
Supplementary Figure 5. A-B. GO analysis of the up / downregulated DEGs involved in MFT samples regarding biological process, cellular component, and molecular function; C. KEGG analysis of the downregulated DEGs involved in MFT samples



Supplementary Figure 6. A-B. q-PCR and western blot of NFIA overexpression efficiency in HepG2; C-D. q-PCR of NFIA interfering efficiency; E. q-PCR of APOA1 in HepG2; F. q-PCR of APOE in HepG2


A
Albumin_urine (ug/mL)
Creatinine_urine (mg/dL)
White blood cell count (1000 cells/uL)
Lymphocyte percent(%)
Lymphocyte number ((1000 cells/uL)
Segmented neutrophils num (1000 cells/uL)
Red cell distribution width (%)
Mean platelet volume (fL)
Blood lead (umol/L)
Folate_serum (nmol/L)
Homocysteine(umol/L)
Folate_RBC (nmol/L RBC)
Cotinine_Serum (ng/mL)
gamma-tocopherol (umol/L)
Retinol (umol/L)
Alkaline Phosphatase (ALP) (U/L)
Blood urea nitrogen (mmol/L)
Gamma Glutamyl Transferase (GGT) (U/L)
Iron (umol/L)
Lactate Dehydrogenase (LDH) (U/L)
Uric acid (umol/L)
Creatinine (umol/L)
Potassium (mmol/L)
Globulin (g/L)
trans-lycopene (umol/L)
Vitamin D (nmol/L)
Direct HDL-Cholesterol (mg/dL)
Type 2 diabetes
Mild cognitive impairment
−1
−0.5
0
0.5
1
B
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effects on T2D
SNP effects on HDL-C
C
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on AD
SNP effect on HDL-C
D
ND vs T2D in blood
Log10 Mean of Normalized Count
Log2 Fold Change
Up
Down
None
E
Alzheimer Disease
NES: 2.03
Pvalue: 0.01
Adjusted Pvalue: 0.09
Running Enrichment Score
Ranked List
Rank in Ordered Dataset
F
MR-SNPs
2452
Degs
58
30
1
115
436
GeneCards


A
BMI (kg/m^2)
****
pre
post
B
FBG (mmol/L)
****
pre
post
C
β-HB（mmol/L）
****
pre
post
D
HDL-C (mmol/L)
****
pre
post
E
HDL-C mmol/L
*
***
pre
post
3months
F
HDL-C mmol/L
***
***
pre
post
6months
G
MoCA score
*
Ctrl
T2D
H
MoCA score
**
pre
post
I
T2D&MCI
DSST score
*
pre
post
J
MoCA Δscore
*
*
Ctrl
T2D
MCI
T2D&MCI
K
Relative Expression of NFIA mRNA
***
pre
post


A
Pre vs Post in blood
Log10 Mean of Normalized Count
Log2 Fold Change
Up
Down
None
B
KEGG Pathway Enrichment of Up-regulated Degs
MAPK signaling pathway
PI3K-Akt signaling pathway
Phospholipase D signaling pathway
ECM-receptor interaction
Aldosterone-regulated sodium reabsorption
Circadian entrainment
Hematopoietic cell lineage
Biosynthesis of unsaturated fatty acids
Regulation of actin cytoskeleton
Transcriptional misregulation in cancer
Fatty acid metabolism
Ras signaling pathway
Adherens junction
Focal adhesion
Prostate cancer
Rap1 signaling pathway
Choline metabolism in cancer
Calcium signaling pathway
Alcoholism
Cocaine addiction
Pathways
Gene Number
pvalue
Count
C
HDL-C(mmol/gprot)
OE-NC OE-NFIA
D
OE-NC
OE-NFIA
GAPDH
IκBα
p-IκBα
p65
p-p65
37
39
39
65
65
E
Relative protein level (p-p65/p65)
OE-NC
OE-NFIA
F
Relative protein level (p-IκBα/IκBα)
OE-NC
OE-NFIA
G
APOA1 (ng/ml)
HepG2 si-NFIA
H
APOA1 (ng/ml)
SH-SY5Ysi-NFIA
I
APOE (ng/ml)
HepG2 si-NFIA
J
APOE (ng/ml)
SH-SY5Ysi-NFIA