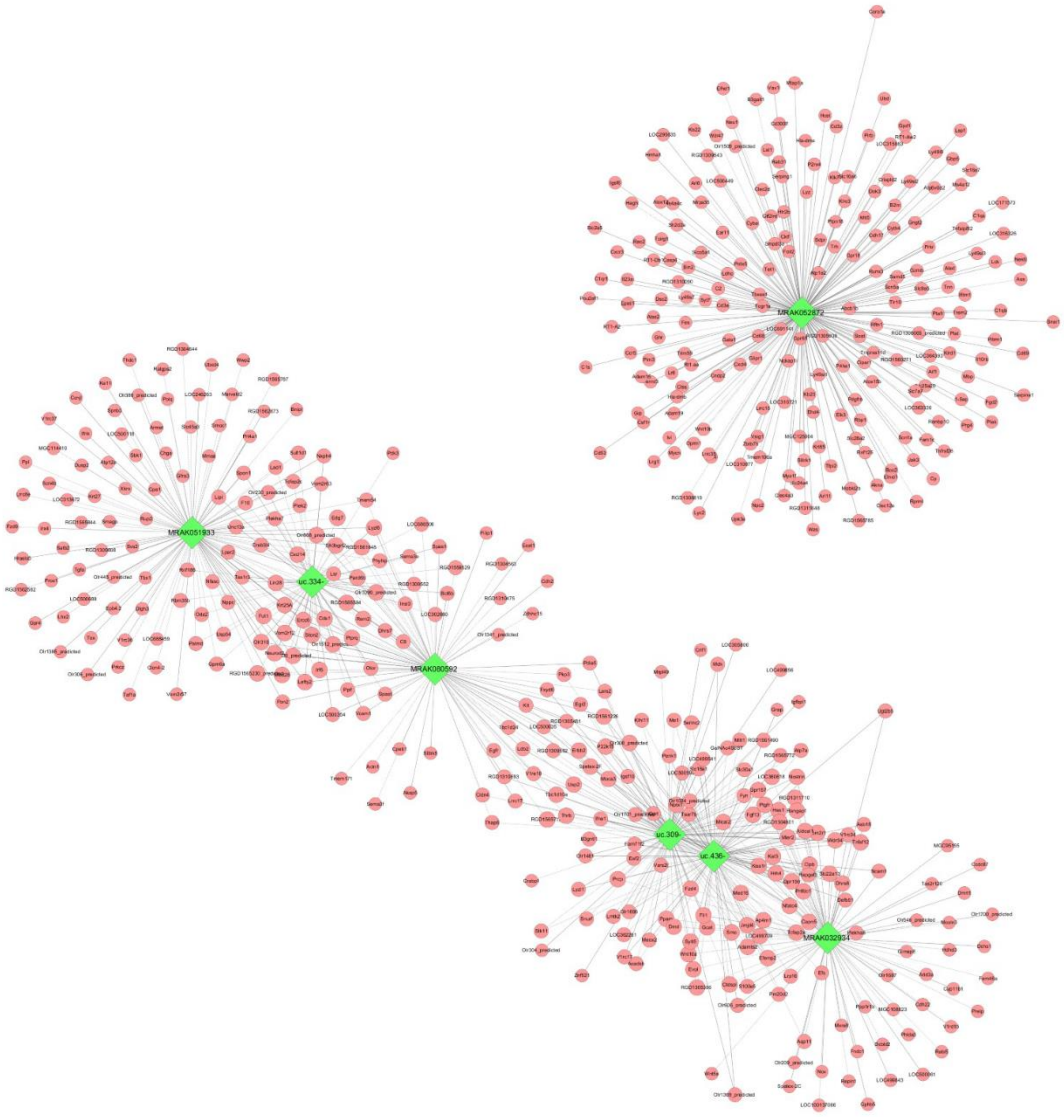
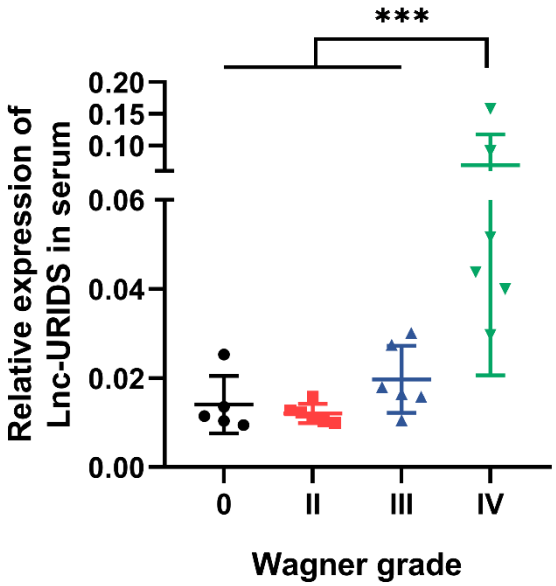
Supplementary Figure S1. LncRNA/mRNA co-expression network. The network represents the co-expression correlations between 7 upregulated lncRNAs and mRNAs (Pearson correlation coefficient ≥ 0.99). Diamonds indicate lncRNAs and circles indicate mRNA transcripts. Solid lines indicate positive correlations, and dashed lines indicate negative correlations.



Supplementary Figure S2. Relative expression of lnc-URIDS in serum of T2DM patients with or without diabetic foot ulcers. RNA expression levels of lnc-URIDS in serum of T2DM patients with different Wagner grades were analyzed by real-time PCR. Data were log transformed before statistical analysis. Data were represented as mean ± SD (n = 5-6). *P < 0.001.



Supplementary Figure S3. The non-coding nature of lnc-URIDS. (A) Putative protein possibly encoded by lnc-URIDS were predicted using ORF Finder. (B) The RNA sequence of lnc-URIDS was put into the Coding Potential Calculator (CPC) program, and was predicted to be non-coding RNAs.

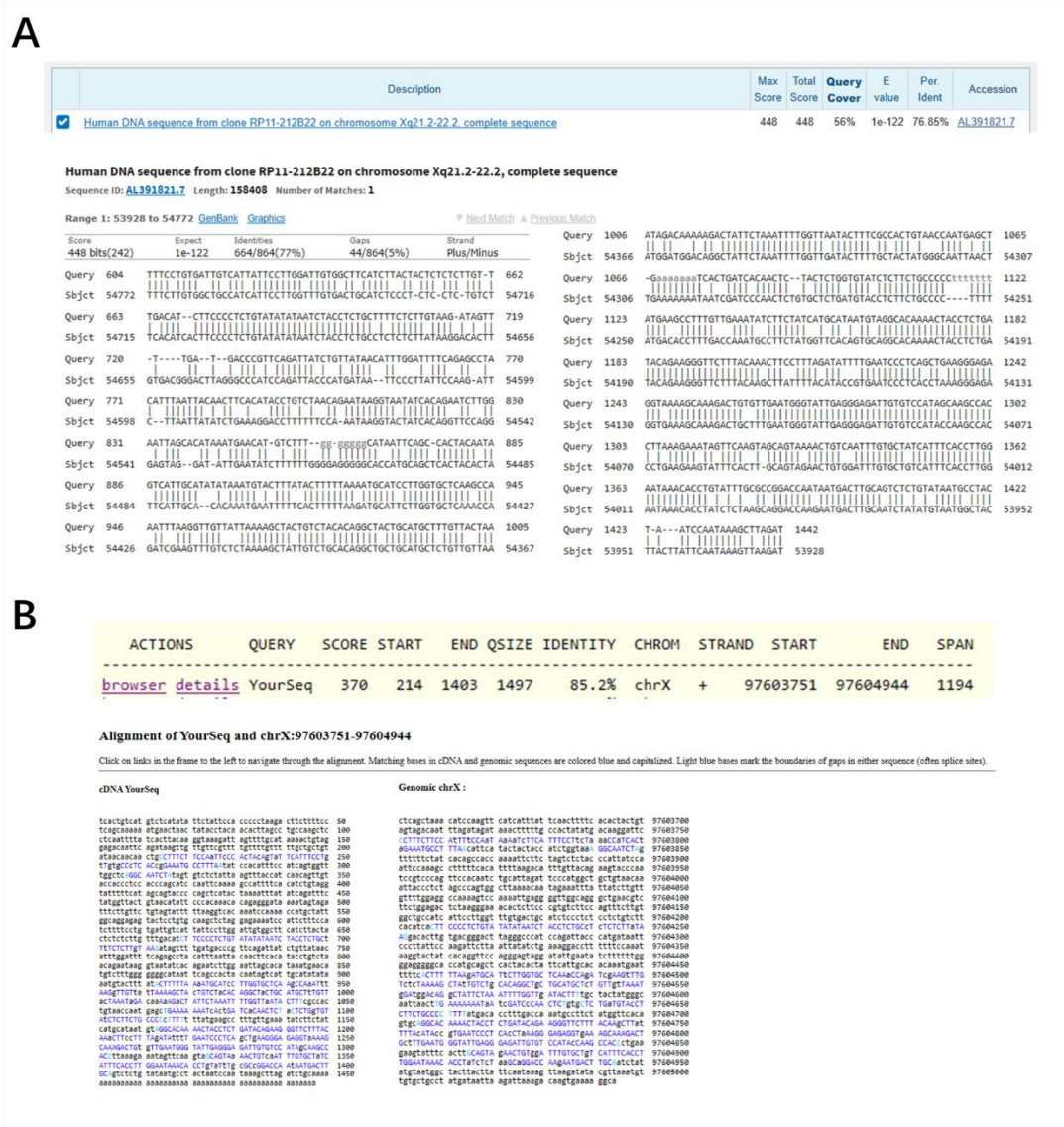
A

Label	Strand	Frame	Start	Stop	Length (nt | aa)
ORF1	**+**	**1**	**268**	**399**	**132 | 43**
ORF4	+	3	543	665	123 | 40
ORF3	+	2	1394	>1495	102 | 33
ORF5	+	3	1152	1235	84 | 27
ORF2	+	1	844	921	78 | 25
ORF8	-	3	292	35	258 | 85
ORF6	-	2	1292	1197	96 | 31
ORF7	-	2	890	798	93 | 30

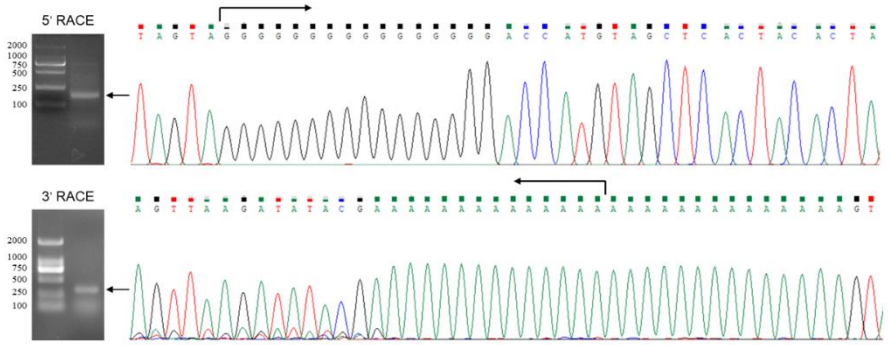
B

ID	C/NC	CODING POTENTIAL SCORE	EVIDENCE	UTR-DB HITs	RNA-DB HITs
MRAK052872	noncoding	-1.04382	detail	search	search

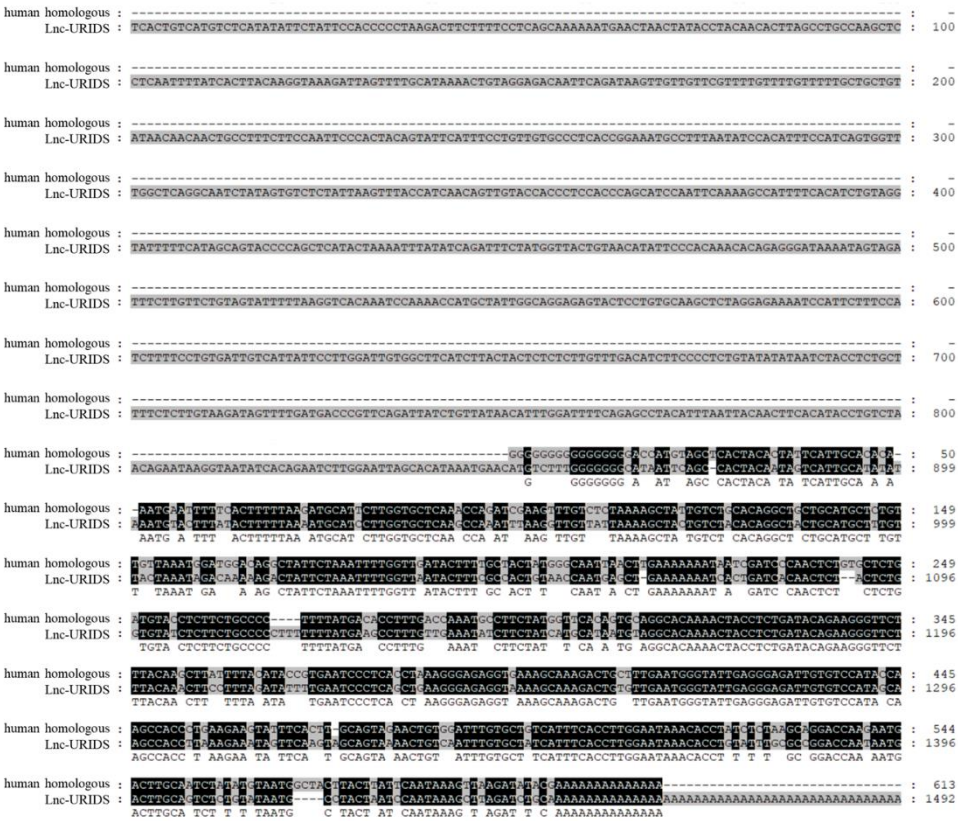
Supplementary Figure S4. Identification of human homologous sequences of lnc-URIDS. (A and B) Searching for human homologous sequences using the NCBI-BLAST (A) and UCSC-BLAT (B). (C) Full length of human homologous sequences of lnc-URIDS in human fibroblasts was performed by RACE. (D) Multiple sequence alignment of lnc-URIDS and its human homologous sequence.



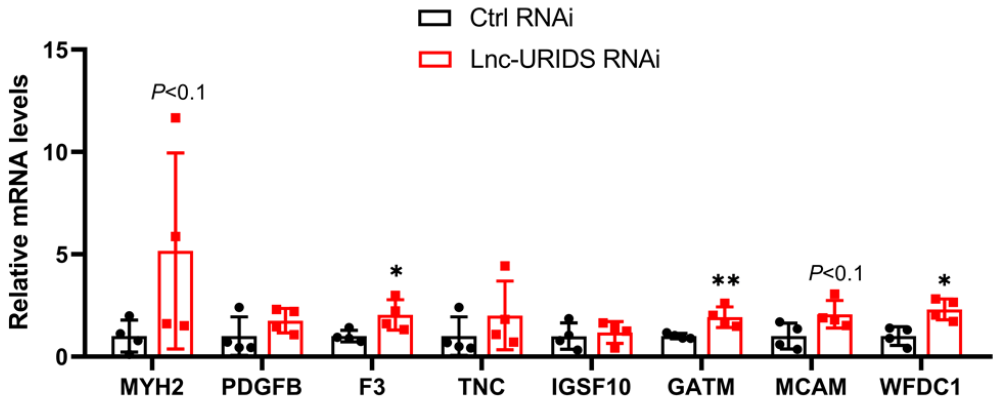
C


5' RACE
2000
1000
750
500
250
100
3' RACE
2000
1000
750
500
250
100

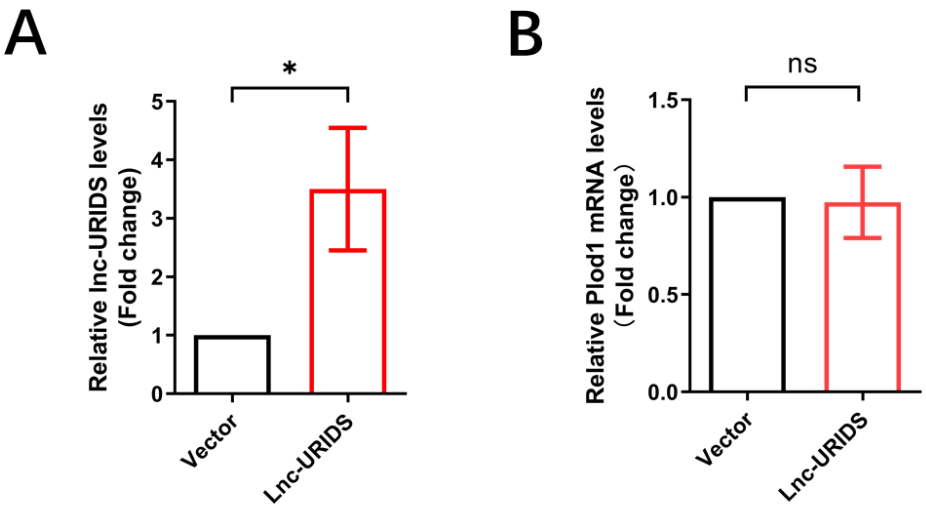
D


human homologous :
Lnc-URIDS :

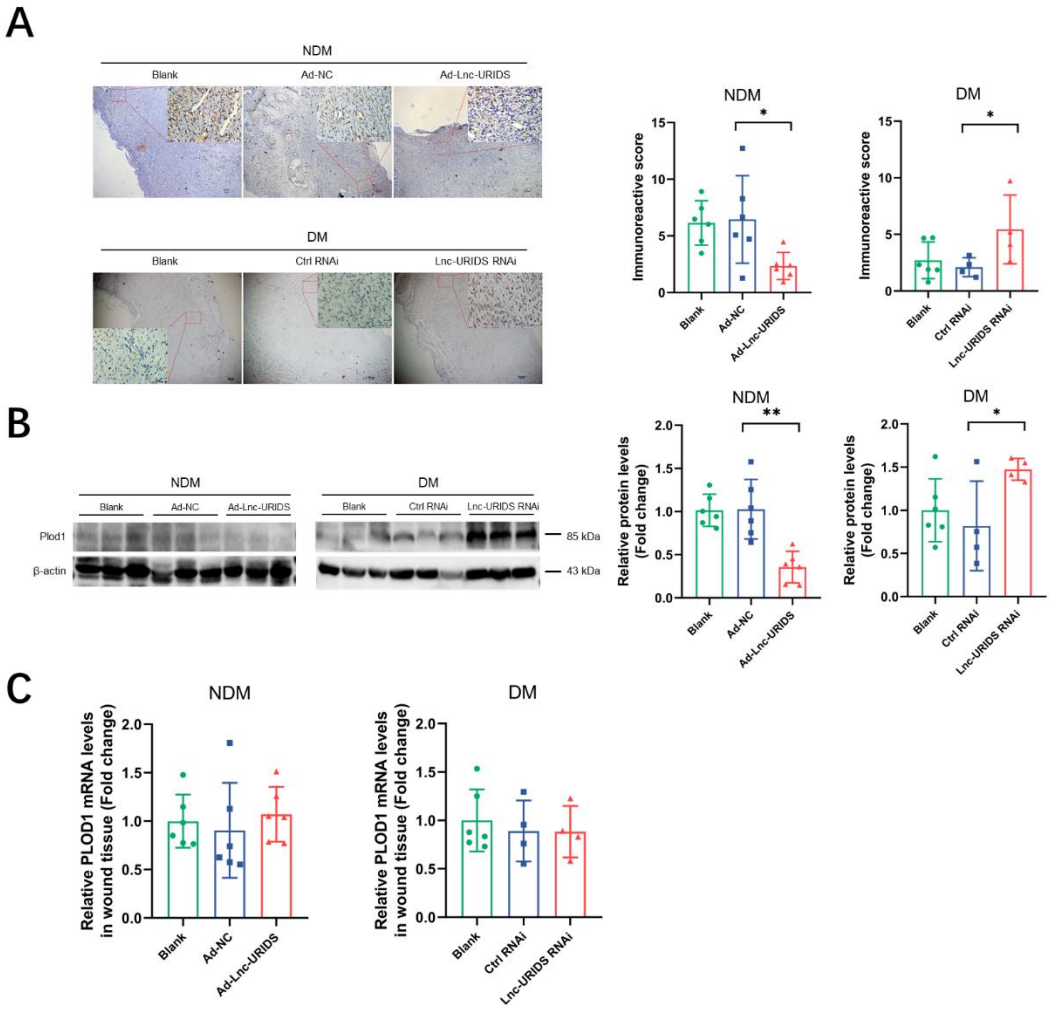
Supplementary Figure S5. Validation of the differentially expressed genes in microarray assay. The mRNA levels of differentially expressed genes that were enriched in wound healing biological process term in microarray assay were examined by real-time PCR. Data were log transformed before statistical analysis. Data were represented as mean ± SD (n = 4). *$P < 0.05$ and **$P < 0.01$.



Supplementary Figure S6. Overexpression of lnc-URIDS showed no effect on the mRNA levels of Plod1. Real-time PCR analysis of lnc-URIDS (A) and Plod1 (B) expression in dermal fibroblasts after overexpression of lnc-URIDS by adenovirus. Data were represented as mean ± SD (n = 3). *$P < 0.05$, ns: not significant.



Supplementary Figure S7. Lnc-URIDS negatively regulates the protein expression of Plod1 in skin wound. (A) IHC of Plod1 in skin tissues from normal wound and diabetic wound. The quantitative analysis of Plod1 was performed according to the immunoreactive score. (B) Western blot analysis of Plod1 in skin tissues from normal wound and diabetic wound. (C) Real-time PCR analysis of Plod1 mRNA expression in skin tissues from normal wound and diabetic wound. Data were represented as mean ± SD (n = 4-6). *$P < 0.05$ and **$P < 0.01$.



Supplemental Tables

Supplementary Table 1. Sequence of primers

Name	Sequence of primers(5'-3')	
Real time-PCR	Forward	Reverse
ACTB	CGAGTACAACCTTCTTGCAGC	ACCCATACCCACCATCACAC
lnc-URIDS	CTCTACTCTGGTGTATCTCTTCTGC	TCCCTCAATACCCATTCAACAC
Plod1	ACGGCTCCTGATTGAGCAAA	CGTAGTACCCATCCGCACTC
RACE	Outer PCR	Inner PCR
3'RACE	TAAGGTTGTTATTAAAAGCTAC	CAACTCTACTCTGGTGTATCTC
5'RACE	CAGGAAAAGATGGAAAGAATGGA	CCTCTGTGTTTGTGGGAATATGT

Supplementary Table 2. Antibodies used

Name of Antibody	Manufacturer, Catalog No	Dilution Used
Anti-Collagen I Rabbit pAb	Servicebio, GB11022-2	1:2000
Anti-Collagen III Rabbit pAb	Servicebio, GB111323	1:2000
PLOD1 Polyclonal Antibody	Thermo Fisher Scientific, PA5-61892	1:2000
ACTB Antibody	Affinity, AF7018	1:2000
Goat Anti-Rabbit IgG (H+L) HRP	Affinity, S0001	1:5000
Goat Anti-Mouse IgG (H+L) HRP	Affinity, S0002	1:5000

Supplementary Table 3. Demographic and clinical characteristics of T2DM patients with different Wagner grades

	Wagner grade				*P*
	0 (n=5)	II (n=6)	III (n=6)	IV (n=6)	
Gender (Male)	4 (80%)	5 (83.33%)	3 (50%)	5 (83.33%)	0.488
Age (year)	59 ± 7	65 ± 19	67 ± 13	65 ± 12	0.814
FBG (mmol/L)	6.0 ± 2.6	6.6 ± 2.1	9.9 ± 3.6	7.0 ± 4.5	0.362
HbA1c (%)	9.7 ± 3.1	8.1 ± 1.8	8.8 ± 2.5	8.8 ± 3.0	0.798
HbA1c(mmol/mol)	83 ± 34	65 ± 20	72 ± 28	72 ± 33	0.798
SBP (mmHg)	126 ± 16	130 ± 26	122 ± 24	126 ± 31	0.656
DBP (mmHg)	78 ± 6	70 ± 6	71 ± 10	69 ± 14	0.967
TC (mmol/L)	4.8 ± 2.5	3.6 ± 0.5	3.5 ± 0.8	3.4 ± 1.0	0.333
TG (mmol/L)	1.1 (0.9, 2.5)	0.9 (0.6, 1.7)	0.9 (0.8, 1.6)	1.0 (1.0, 1.6)	0.022
LDL-C (mmol/L)	2.8 ± 1.4	2.2 ± 0.4	2.3 ± 0.7	2.3 ± 0.7	0.268
HDL-C (mmol/L)	0.9 ± 0.4	1.0 ± 0.2	0.8 ± 0.2	0.6 ± 0.3	0.647
CRE (μmol/L)	93 ± 29	136 ± 73	83 ± 22	218 ± 119	0.862
RBC ($\times 10^{12}$/L)	4.2 ± 3.7	3.6 ± 0.9	3.7 ± 0.8	3.2 ± 0.7	0.138
WBC ($\times 10^{9}$/L)	8.5 ± 2.5	7.8± 1.6	9.8 ± 2.9	11.2 ± 5.6	0.156
PLT ($\times 10^{9}$/L)	321 ± 162	279 ± 99	373 ± 122	416 ± 144	0.389
HGB (g/L)	126 ± 15	107 ± 22	100 ± 23	81 ± 17	0.011

Continuous variables are presented as mean ± SD for parametric variables and median (interquartile range) for nonparametric variables. Categorical variables are presented as numbers (proportions). FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; CRE, creatinine; RBC, red blood cell; WBC, white blood cell; PLT, blood platelet; HGB, hemoglobin.

Supplementary Table 4. Criteria of preliminary screening and characterization of 7 upregulated lncRNAs

SeqID	Absolute Fold change ([Test] vs [Ctrl])	source	chromosome	strand	relationship
MRAK032934	2.043212031	mouse_ortholog	chr10	-	antisense
MRAK051933	2.264423067	mouse_ortholog	chr13	-	intergenic
MRAK052872	2.309756272	mouse_ortholog	chrX	+	intergenic
MRAK080592	2.752328174	mouse_ortholog	chr7	-	intergenic
uc.309-	3.78374103	UCR	chr1	-	antisense
uc.334-	2.223166345	UCR	chr8	+	antisense
uc.436-	2.993645207	UCR	chr18	+	intergenic

Criteria:

Abundance: Average microarray raw intensity > 50 in NDM group;

Length: 200 nt < lncRNA length < 5000 nt;

Coding capability: ORF Finder < 100 amino acids and coding potential score < 0;

Relationship of lncRNA and its nearby coding gene: antisense/intergenic;

Conservation: Human homologous.

Supplementary Table 5. GO biological process enrichment analysis of the mRNAs co-expressed with 7 lncRNAs

LncRNA	Term	P-value	Gene Counts
MRAK032934	wound healing	0.069	3
MRAK051933	wound healing	/	/
MRAK052872	wound healing	0.021	5
MRAK080592	wound healing	/	/
uc.309-	wound healing	/	/
uc.334-	wound healing	/	/
uc.436-	wound healing	/	/