Supplementary Figure S1. LncRNA/mRNA co-expression network. The network represents the co-expression correlations between 7 upregulated lncRNAs and mRNAs (Pearson correlation coefficient  $\geq$  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 Inc-URIDS in serum of T2DM patients with or without diabetic foot ulcers. RNA expression levels of Inc-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  $\pm$  SD (n = 5-6). \*P < 0.001.



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

А

| 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          |

В

| 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.

|  |  |   |  |  | Description   | 1  |  |   |   |  |  | Max<br>Score  | Total<br>Score  | Query<br>Cover  | E<br>value   | Per.<br>Ident  | Access  |
|--|--|---|--|--|---|--|--|---|---|--|--|---|---|---|--|--|---|
| 🖌 Н  | uman DNA   | sequence from c   | lone RP11-212B22   | on chromoso  | me Xq21.2-7   | 22.2, compl  | ete sequen                                   | ce  |   |  |  | 448   | 448   | 56%   | 1e-122   | 76.85%   | AL39182   |
| Huma<br>Sequery<br>Range<br>Score<br>448 b<br>Query<br>Sbjct<br>Query<br>Sbjct | an DNA s<br>nce ID: AL3<br>e 1: 53928<br>bits(242)<br>604<br>: 54772<br>663<br>: 54715 | Expect   1e-122   THECTRATIST   Expect   1e-122   THECTRATIST   THECTRATIST | Ilone RP11-212E  | Gaps<br>44/86-<br>GTGGCTTCATC<br>GTGGCTTCATC<br>GTGGCTTCATC<br>GTGGCTTCATC<br>GTGCTCTGCT<br>CTACCTCTGCCT | 4(5%)<br>4(5%)<br>CTTACTACTCT<br>11 11 111<br>CTCCCT-CTC-<br>TTTCTCTTGT/<br>TCTCTCTTAT/                       | Strand<br>Plus/Minu<br>rCTCTTGT-T<br>III III I<br>-CTC-TGTCT<br>AAG-ATAGTT<br>AAGGACACTT                             | 2, comple                                    | vious Match<br>Query<br>Sbjct<br>Query<br>Sbjct<br>Query<br>Sbjct | 1006<br>54366<br>1066<br>54306<br>1123<br>54250 | ATAGACAA<br>     <br>ATGGATGG<br>-Gaaaaaa<br>      <br>TGAAAAAA<br>ATGAAGCC<br>        | AAAGACTAT<br>          <br>ACAGGCTAT<br>        <br>ATAATCGAT<br>       <br> | TCTAAAT<br>       <br>TCTAAAT<br>CACAACTI<br>      <br>CCCAACTI<br>ATATCTTI<br>      <br>ATGCCTTI | TTTGGTT<br>IIIIIII<br>TTTGGTT<br>CTACT<br>IIIII<br>CTGTGCT<br>CTATCAT<br>IIIII<br>CTATGGT | AATACTT<br>      <br>GATACTT<br>CTGGTGT/<br>      <br>CTGATGT/<br>GCATAAT(<br>     <br>TCACAGT( | TCGCCACT<br>IIIII<br>TTGCTACT<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTT(<br>ATCTCTTCTT(<br>ATCTCTTCTT(<br>ATCTCTTCTT(<br>ATCTCTTCTTCTT(<br>ATCTCTTCTTCTTCTTCTT(<br>ATCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT | TGTAACCA<br>      <br>TATGGGCA<br>CTGCCCCC<br>       <br>CTGCCCC-<br>CAAAACTA<br>        <br>AAAACTA | ATGAGCT<br>       <br>ATTAACT<br>tttttt<br>TTTT<br>CCTCTGA                          |
| Query<br>Sbjct<br>Query<br>Sbjct<br>Query<br>Sbjct                             | 720<br>54655<br>771<br>54598<br>831<br>54541   | -TTGAT<br>     <br>GTGACGGGACTTAG<br>CATTTAATTACAAC<br>         <br>CTTAATTATAC<br>AATTAGCACATAAA<br>        <br>GAGTAGGAT-AT   | GACCCGTTCAGATTAT<br>             <br>AGGCCCATCCAGATTAC<br>TTCACATACCTGTCTA<br>          <br>TGAAAGGACCTTTTTT<br>ATGAACAT-GTCTTT<br>              <br>TGAATATCTTTTTGG | CTGTTATAAC/<br>.CCATGATAA<br>LACAGAATAAG(<br>  | TTTGGATTTT<br>-TTCCCTTATT<br>STAATATCACA<br>III IIIIII<br>STACTATCACA<br>FAATTCAGC-(<br>IIIIII<br>CCATGCAGCT( | TCAGAGCCTA<br>       <br>TCCAAG-ATT<br>AGGATCTTGG<br>        <br>AGGTTCCAGG<br>CACTACAATA<br>         <br>CACTACACTA | 770<br>54599<br>830<br>54542<br>885<br>54485 | Query<br>Sbjct<br>Query<br>Sbjct<br>Query<br>Sbjct                | 1183<br>54190<br>1243<br>54130<br>1303<br>54070 | TACAGAAGG<br>TACAGAAGG<br>GGTAAAAGG<br>III IIII<br>GGTGAAAGG<br>CTTAAAGAA<br>CCTGAAGAA | SGTTCTTTA<br>SGTTCTTTA<br>CAAAGACTG<br>IIIIIIIII<br>CAAAGACTG<br>AATAGTTCA   | CAAACTT<br>III III<br>CAAGCTT<br>TGTTGAA<br>IIIII<br>CTTTGAA<br>AGTAGCA<br>IIII<br>CTT-GCA        | CCTTTAG<br>ATTTTAC<br>TGGGTAT<br>IIIIIII<br>TGGGTAT<br>STAAAAC<br>III III<br>STAGAAC      | ATATTTT<br>ATACCGT<br>TGAGGGA<br>TGAGGGA<br>TGAGGGA<br>TGTCAAT<br>III II<br>TGTGGAT             | SAATCCC<br>SAATCCC<br>SATTGTG<br>SATTGTG<br>SATTGTG<br>TTGTGCTA  | TCAGCTGA<br>IIIIII<br>TCACCTAA<br>TCCATAGC<br>IIIIIII<br>TCCATACC<br>ATCATTTC<br>IIIIIII<br>STCATTTC | AGGGAGA<br>AGGGAGA<br>AAGCCAC<br>IIIIIII<br>AAGCCAC<br>ACCTTGG<br>IIIIII<br>ACCTTGG |
| Query<br>Sbjct<br>Query<br>Sbjct   | 886<br>54484<br>946<br>54426   | GTCATTGCATATAT.<br>        <br>TTCATTGCACAC<br>AATTTAAGGTTGTT.<br>      <br>GATCGAAGTTTGTC  | AAATGTACTTTATACT   | TTTTAAAATGO  | CATCCTTGGTC   | SCTCAAGCCA<br>         <br>SCTCAAACCA<br>ITTGTTACTAA<br>        <br>CTGTTGTTAA                                       | 945<br>54427<br>1005<br>54367                | Query<br>Sbjct<br>Query<br>Sbjct                                  | 1363<br>54011<br>1423<br>53951                  | ААТАААСА<br>        <br>ААТАААСАС<br>Т-ААТС<br>   АТС<br>ТТАСТТАТ                      | CCTGTATTT<br>         <br>CCTATCTCT<br>CCAATAAAG<br>       <br>TCAATAAAG     | GCGCCGG<br>     <br>AAGCAGG<br>CTTAGAT<br>      <br>TTAAGAT                                       | ACCAATA<br>       <br>ACCAAGA<br>1442<br>53928  | ATGACTTO  | SCAGTCT(<br>SCAATCT)   | TGTATAA  | TGCCTAC   |
|  | A  | TIONS   | QUERY  | SCORE  | START   | END Q  | SIZE   | IDENTI  | TY (  | HROM   | STRAN  | D ST  | TART  |   | END  | SF   | AN  |
|  |  |   | s YourSeq  | 370  | 214   | 1403   | 1497   | 85.   | 2% (  | hrX  | +  | 97603   | 3751  | 9766  | 04944  | 11   | .94   |
|  | Alignm   | ent of YourSeq  | and chrX:9760  | 03751-9760<br>te alignment. Ma   | )4944<br>tching bases in (  | cDNA and gen   | omic sequenc                                 | es are colored  | blue and ci                                     | pitalized. Ligh  | t blue bases :   | nark the bo   | undaries of   | f gaps in eit   | ber sequen   | ce (often spl  | ice sites).   |
|  | Alignm<br>Click on lin   | ent of YourSeq<br>ks in the frame to the h<br>Seq   | and chrX:9760  | 03751-9760<br>te alignment. Ma   | )4944<br>tching bases in<br>Genomic   | cDNA and gen   | omic sequenc                                 | es are colored  | blue and c                                      | pitalized. Ligh  | t blue bases r   | nark the bo   | undaries of   | f gaps in eit   | her sequen   | ce (often spl  | ice sites).   |



### 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  $\pm$  SD (n = 4). \**P* < 0.05 and \*\**P* < 0.01.



Supplementary Figure S6. Overexpression of Inc-URIDS showed no effect on the mRNA levels of Plod1. Real-time PCR analysis of Inc-URIDS (A) and Plod1 (B) expression in dermal fibroblasts after overexpression of Inc-URIDS by adenovirus. Data were represented as mean  $\pm$  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  $\pm$  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     |
| Inc-URIDS     | CTCTACTCTGGTGTATCTCTTCTGC  | TCCCTCAATACCCATTCAACAC   |
| Plod1         | ACGGCTCCTGATTGAGCAAA       | CGTAGTACCCATCCGCACTC     |
| RACE          | Outer PCR                  | Inner PCR                |
| 3'RACE        | TAAGGTTGTTATTAAAAGCTAC     | CAACTCTACTCTGGTGTATCTC   |
| 5'RACE        | CAGGAAAAGATGGAAAGAATGGA    | CCTCTGTGTTTGTGGGGAATATGT |

| Supponentary fusic 2. finitioules 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 2. Antibodies used

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

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

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, lowdensity lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; CRE, creatinine; RBC, red blood cell; WBC, white blood cell; PLT, blood platelet; HGB, hemoglobin.

|            | Absolute Fold  |                |            |        |              |
|------------|----------------|----------------|------------|--------|--------------|
| SeqID      | change ([Test] | source         | chromosome | strand | relationship |
|            | vs [Ctrl])     |                |            |        |              |
| 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   |

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

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.

| 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 | /       | /           |

Supplementary Table 5. GO biological process enrichment analysis of the mRNAs coexpressed with 7 lncRNAs