**Supplementary Table S1.** Linkage disequilibrium tests (D’ and r2)

|  |  |  |  |
| --- | --- | --- | --- |
| D’ | B5 | B8 | PuvII |
| Xba1 | 0.062 | 0.267 | 0.074 |
| B5 | - | 0.027 | 0.263 |
| B8 | - | - | 0.040 |
| r2 | B5 | B8 | PuvII |
| Xba1 | 0.002 | 0.034 | 0.005 |
| B5 | - | ＜0.001 | 0.035 |
| B8 | - | - | 0.001 |

The estimation of LD for all pairs SNP makers showed that XbaI and PvuII of ESRl were in a relatively relationship with the standardized D’=0.074，as well as RsaI (B5) and AluI (B8) of ESR2 with the standardized D’=0.027.

**Supplementary Table S2.** Relationship between Xba1 genotypes and clinical indicators within each group

|  |  |  |  |
| --- | --- | --- | --- |
| 　 | AA  | AG  | GG  |
| Total | n=74 | n=154 | n=76 |
| Age (years) | 62.14±4.24 | 63.24±4.85 | 63.11±3.75 |
| **BMI (kg/m2)** | **22.97±2.99** | **23.98±3.40** | **24.71±3.18\*** |
| Waist circumference (cm) | 84.26±5.36 | 84.92±5.13 | 86.07±4.96 |
| **FBG (mmol/L)** | **5.82±1.42** | **6.08±1.51** | **6.43±1.33\*** |
| HbA1C (%) | 5.89±1.00 | 5.94±1.05 | 6.09±0.98 |
| **SBP (mmHg)** | **132.31±14.39** | **134.15±13.96** | **139.05±14.12\*#** |
| **DBP (mmHg)** | **79.95±11.96** | **81.14±11.39** | **85.86±10.69\*#** |
| **TG (mmol/L)** | **1.84±0.92** | **2.08±1.20** | **2.38±1.16\*** |
| **TC (mmol/L)** | **4.29±1.20** | **4.72±0.83\*** | **5.53±1.12\*#** |
| **HDL-C (mmol/L)** | **1.25±0.26** | **1.15±0.21\*** | **1.06±0.20\*#** |
| **LDL-C (mmol/L)** | **2.74±0.64** | **2.83±0.67** | **3.39±0.83\*#** |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| Fasting serum insulin (μIU/mL) | 11.15±5.68 | 11.54±6.23 | 12.54±8.31 |
| Estradiol (pg/ml) | 26.82±6.99 | 24.66±7.67 | 24.49±7.67 |
| **HOMA-IR** | **2.47±1.32** | **2.72±1.77** | **3.20±1.70\*** |
| MetS | n=29 | n=73 | n=48 |
| Age (years) | 61.93±3.70 | 63.55±4.37 | 62.88±3.81 |
| **BMI (kg/m2)** | **24.15±3.53** | **25.46±2.73** | **25.98±2.68\*** |
| Waist circumference (cm) | 87.31±7.18 | 88.59±4.69 | 88.33±4.68 |
| FBG (mmol/L) | 7.03±1.39 | 7.14±1.41 | 6.96±1.39 |
| HbA1C (%) | 6.91±0.76 | 6.80±0.87 | 6.52±0.95 |
| SBP (mmHg) | 148.52±6.98 | 147.34±7.21 | 148.88±6.41 |
| DBP (mmHg) | 93.34±4.50 | 91.77±4.65 | 93.04±4.23 |
| **TG (mmol/L)** | **1.94±0.72** | **2.35±1.02** | **2.67±1.18\*** |
| **TC (mmol/L)** | **4.77±1.26** | **4.89±0.77** | **5.48±1.09\*#** |
| HDL-C (mmol/L) | 0.96±0.08 | 0.97±0.14 | 0.96±0.17 |
| **LDL-C (mmol/L)** | **3.03±0.80** | **2.84±0.78** | **3.41±0.88#** |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| Fasting serum insulin (μIU/mL) | 14.28±6.60 | 14.04±6.21 | 14.63±8.89 |
| Estradiol (pg/ml) | 23.31±5.51 | 23.12±7.63 | 23.25±7.68 |
| HOMA-IR | 3.18±1.50 | 3.45±1.90 | 3.63±1.76 |
| Control | n=45 | n=81 | n=28 |
| Age (years) | 62.27±4.58 | 62.96±5.26 | 63.50±3.68 |
| BMI (kg/m2) | 22.20±2.31 | 22.65±3.40 | 22.55±2.82 |
| Waist circumference (cm) | 82.29±2.17 | 81.62±2.68 | 82.18±2.36 |
| **FBG (mmol/L)** | **5.04±0.73** | **5.13±0.78** | **5.50±0.40\*** |
| HbA1C (%) | 5.22±0.40 | 5.17±0.38 | 5.35±0.44 |
| SBP (mmHg) | 121.87±5.29 | 122.26±4.91 | 122.21±4.10 |
| DBP (mmHg) | 71.31±5.48 | 71.57±5.72 | 73.54±6.10 |
| TG (mmol/L) | 1.78±1.03 | 1.83±1.29 | 1.88±0.96 |
| **TC (mmol/L)** | **3.99±1.07** | **4.56±0.85\*** | **5.61±1.19\*#** |
| **HDL-C (mmol/L)** | **1.44±0.12** | **1.31±0.10\*** | **1.23±0.13\*#** |
| **LDL-C (mmol/L)** | **2.54±0.43** | **2.82±0.55\*** | **3.35±0.75\*#** |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| Fasting serum insulin (μIU/mL) | 9.14±3.90 | 9.28±5.36 | 8.95±5.76 |
| Estradiol (pg/ml) | 29.09±6.95 | 26.05±7.11 | 26.61±7.31 |
| HOMA-IR | 2.02±0.97 | 2.07±1.36 | 2.48±1.48 |

 Continuous data were presented as mean±SD and analyzed by one-way ANOVA and the Bonferroni method for multiple comparisons between groups.

Categorical data are presented as n (%) and analyzed using chi-square test.

\*P<0.05 vs. the AA group

#P<0.05 vs. the AG group

Abbreviations: FBG, fasting blood glucose; HbA1C, hemoglobin A1C; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, Triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NAFLD, non-alcoholic fatty liver disease; HOMA-IR, homeostasis model assessment of insulin resistance.

**Supplementary Table S3.** Relationship between RsaI (B5) genotypes and clinical indicators in each group

|  |  |  |  |
| --- | --- | --- | --- |
| 　 | AA  | AG | GG |
| Total | n=38 | n=124 | n=142 |
| **Age (years)** | **62.00±4.63** | **63.71±4.42\*** | **62.51±4.38** |
| BMI (kg/m2) | 24.05±4.67 | 23.72±3.08 | 24.05±3.04 |
| Waist circumference (cm) | 85.90±4.62 | 84.33±5.19 | 85.44±5.25 |
| FBG (mmol/L) | 6.30±1.72 | 6.10±1.47 | 6.05±1.37 |
| HbA1C (%) | 5.80±0.84 | 5.97±0.99 | 6.01±1.09 |
| SBP (mmHg) | 137.11±14.45 | 134.81±13.80 | 134.45±14.70 |
| DBP (mmHg) | 82.29±12.73 | 82.29±11.82 | 81.73±11.05 |
| **TG (mmol/L)** | **2.52±1.35** | **2.01±1.09\*** | **2.09±1.01** |
| TC (mmol/L) | 4.98±1.01 | 4.79±1.15 | 4.80±1.08 |
| HDL-C (mmol/L) | 1.11±0.23 | 1.16±0.24 | 1.16±0.23 |
| **LDL-C (mmol/L)** | **2.55±0.73** | **3.06±0.80\*** | **2.96±0.68\*** |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| **Fasting serum insulin (μIU/mL)** | **14.86±8.13** | **10.53±5.99\*** | **11.86±6.60\*** |
| Estradiol (pg/ml) | 24.79±9.15 | 25.69±7.23 | 24.76±7.16 |
| **HOMA-IR** | **3.83±2.41** | **2.48±1.51\*** | **2.77±1.45\*** |
| MetS | n=20 | n=61 | n=69 |
| Age (years) | 62.10±3.13 | 63.49±4.25 | 62.87±4.19 |
| BMI (kg/m2) | 25.54±2.81 | 25.57±2.70 | 25.14±3.19 |
| Waist circumference (cm) | 88.80±4.06 | 87.10±5.88 | 89.13±4.79 |
| FBG (mmol/L) | 7.42±1.68 | 7.06±1.38 | 6.96±1.32 |
| HbA1C (%) | 6.35±0.80 | 6.71±0.85 | 6.86±0.92 |
| SBP (mmHg) | 149.45±7.78 | 147.36±7.32 | 148.28±6.28 |
| DBP (mmHg) | 93.40±4.36 | 93.03±4.44 | 91.72±4.58 |
| TG (mmol/L) | 2.63±0.76 | 2.36±1.27 | 2.31±0.90 |
| TC (mmol/L) | 5.01±0.72 | 5.08±1.02 | 5.05±1.11 |
| HDL-C (mmol/L) | 0.93±1.12 | 0.97±0.15 | 0.97±0.14 |
| **LDL-C (mmol/L)** | **2.40±0.71** | **3.28±0.89\*** | **3.07±0.76\*** |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| Fasting serum insulin (μIU/mL) | 17.90±8.96 | 13.89±6.27 | 13.57±7.20 |
| Estradiol (pg/ml) | 25.00±10.91 | 23.82±6.81 | 22.13±6.18 |
| **HOMA-IR** | **4.91±2.71** | **3.28±1.54\*** | **3.18±1.39\*** |
| Control | n=18 | n=63 | n=73 |
| Age (years) | 61.89±5.98 | 63.92±4.60 | 62.18±4.55 |
| BMI (kg/m2) | 22.39±5.76 | 21.93±2.27 | 23.02±2.52 |
| Waist circumference (cm) | 82.67±2.66 | 81.65±2.25 | 81.96±2.63 |
| FBG (mmol/L) | 5.06±0.43 | 5.17±0.80 | 5.20±0.72 |
| HbA1C (%) | 5.18±0.26 | 5.25±0.41 | 5.20±0.42 |
| SBP (mmHg) | 123.39±2.83 | 122.65±4.52 | 121.38±5.44 |
| DBP (mmHg) | 69.94±5.00 | 71.89±5.89 | 72.29±5.76 |
| TG (mmol/L) | 2.40±1.81 | 1.68±1.01 | 1.81±1.05 |
| TC (mmol/L) | 4.96±1.29 | 4.50±1.20 | 4.56±1.00 |
| HDL-C (mmol/L) | 1.30±0.14 | 1.34±0.15 | 1.34±0.12 |
| LDL-C (mmol/L) | 2.71±0.74 | 2.85±0.64 | 2.86±0.58 |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| **Fasting serum insulin (μIU/mL)** | **11.48±5.59** | **7.29±3.37\*** | **10.25±5.57#** |
| Estradiol (pg/ml) | 24.56±7.01 | 27.51±7.20 | 27.25±7.17 |
| **HOMA-IR** | **2.64±1.24** | **1.69±0.99\*** | **2.38±1.42#** |

Continuous data were presented as mean±SD and analyzed by one-way ANOVA and the Bonferroni method for multiple comparisons between groups.

Categorical data are presented as n (%) and analyzed using chi-square test.

\*P<0.05 vs. the AA group

#P<0.05 vs. the AG group

Abbreviations: FBG, fasting blood glucose; HbA1C, hemoglobin A1C; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, Triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NAFLD, non-alcoholic fatty liver disease; HOMA-IR, homeostasis model assessment of insulin resistance.

**Supplementary Table S4.** Relationship between AluI (B8) genotypes and clinical indicators of each group

|  |  |  |  |
| --- | --- | --- | --- |
| 　 | AA | AG | GG |
| Total | n=41 | n=114 | n=149 |
| Age (years) | 61.66±3.40 | 63.01±5.04 | 63.23±4.20 |
| BMI (kg/m2) | 23.12±3.74 | 24.28±3.15 | 23.86±3.25 |
| Waist circumference (cm) | 85.22±5.07 | 84.93±5.51 | 85.09±4.96 |
| FBG (mmol/L) | 5.88±1.42 | 6.09±1.46 | 6.18±1.46 |
| HbA1C (%) | 6.07±0.95 | 6.02±1.08 | 5.90±0.99 |
| SBP (mmHg) | 135.10±14.64 | 135.40±15.30 | 134.52±13.43 |
| DBP (mmHg) | 82.61±12.11 | 82.35±11.57 | 81.62±11.44 |
| TG (mmol/L) | 1.70±0.73 | 2.20±1.13 | 2.13±1.22 |
| **TC (mmol/L)** | **4.22±1.24** | **4.89±1.07\*** | **4.92±1.03\*** |
| HDL-C (mmol/L) | 1.16±0.22 | 1.13±0.24 | 1.17±0.23 |
| **LDL-C (mmol/L)** | **2.68±0.64** | **2.94±0.80** | **3.03±0.73\*** |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| Fasting serum insulin (μIU/mL) | 11.83±5.46 | 11.56±6.52 | 11.75±7.14 |
| Estradiol (pg/ml) | 26.71±6.21 | 25.19±7.72 | 24.68±7.53 |
| HOMA-IR | 2.74±1.37 | 2.60±1.57 | 2.94±1.81 |
| MetS | n=21 | n=58 | n=71 |
| **Age (years)** | **60.95±3.14** | **63.59±4.30\*** | **63.17±4.03** |
| BMI (kg/m2) | 25.14±3.90 | 25.91±2.90 | 25.00±2.60 |
| Waist circumference (cm) | 87.90±5.40 | 87.88±6.01 | 88.68±4.51 |
| FBG (mmol/L) | 6.70±1.35 | 7.08±1.30 | 7.15±1.48 |
| HbA1C (%) | 6.76±0.77 | 6.81±0.93 | 6.66±0.88 |
| SBP (mmHg) | 147.33±8.01 | 149.28±6.73 | 147.28±6.66 |
| DBP (mmHg) | 93.24±4.30 | 92.47±4.70 | 92.27±4.47 |
| **TG (mmol/L)** | **1.57±0.54** | **2.39±1.09\***  | **2.60±1.02\*** |
| TC (mmol/L) | 4.67±1.16 | 5.07±0.97 | 5.16±1.02 |
| HDL-C (mmol/L) | 0.97±0.07 | 0.94±0.15 | 0.98±0.15 |
| LDL-C (mmol/L) | 2.70±0.66 | 3.05±0.89 | 3.18±0.85 |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| Fasting serum insulin (μIU/mL) | 13.65±4.29 | 14.76±6.77 | 14.06±8.21 |
| Estradiol (pg/ml) | 26.33±6.04 | 23.35±6.63 | 22.16±7.83 |
| HOMA-IR | 3.15±1.03 | 3.36±1.67 | 3.62±1.99 |
| Control | n=20 | n=56 | n=78 |
| Age (years) | 62.40±3.59 | 62.41±5.69 | 63.29±4.38 |
| **BMI (kg/m2)** | **20.99±2.06** | **22.58±2.44** | **22.83±3.45\*** |
| Waist circumference (cm) | 82.40±2.64 | 81.88±2.49 | 81.82±2.46 |
| FBG (mmol/L) | 5.02±0.89 | 5.05±0.73 | 5.30±0.66 |
| HbA1C (%) | 5.35±0.45 | 5.20±0.39 | 5.20±0.39 |
| SBP (mmHg) | 122.25±6.66 | 121.02±4.54 | 122.91±4.45 |
| DBP (mmHg) | 71.45±5.77 | 71.88±5.72 | 71.94±5.81 |
| TG (mmol/L) | 1.84±0.88 | 2.00±1.14 | 1.70±1.23 |
| **TC (mmol/L)** | **3.74±1.16** | **4.71±1.14\*** | **4.71±1.01\*** |
| HDL-C (mmol/L) | 1.36±0.11 | 1.32±0.15 | 1.34±0.13 |
| LDL-C (mmol/L) | 2.66±0.63 | 2.82±0.68 | 2.90±0.57 |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| Fasting serum insulin (μIU/mL) | 9.93±5.99 | 8.25±4.24 | 9.66±5.25 |
| Estradiol (pg/ml) | 27.10±6.51 | 27.11±8.34 | 26.97±6.50 |
| HOMA-IR | 2.31±1.57 | 1.80±0.96 | 2.32±1.37 |

Continuous data were presented as mean±SD and analyzed by one-way ANOVA and the Bonferroni method for multiple comparisons between groups.

Categorical data are presented as n (%) and analyzed using chi-square test.

\*P<0.05 vs. the AA group

#P<0.05 vs. the AG group

Abbreviations: FBG, fasting blood glucose; HbA1C, hemoglobin A1C; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, Triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NAFLD, non-alcoholic fatty liver disease; HOMA-IR, homeostasis model assessment of insulin resistance.

**Supplementary Table S5.** Relationship between PVUII genotypes and clinical indicators in each group

|  |  |  |  |
| --- | --- | --- | --- |
| 　 | TT | TC | CC |
| Total | n=69 | n=163 | n=72 |
| Age (years) | 63.14±5.92 | 63.07±4.02 | 62.43±3.76 |
| **BMI (kg/m2)** | **25.17±3.69** | **23.21±3.15\*** | **24.32±2.79#** |
| Waist circumference (cm) | 84.93±4.72 | 85.07±5.69 | 85.10±4.34 |
| FBG (mmol/L) | 5.86±1.35 | 6.11±1.43 | 6.32±1.57 |
| HbA1C (%) | 5.96±1.08 | 5.94±1.01 | 6.02±0.98 |
| SBP (mmHg) | 133.12±12.02 | 134.80±14.80 | 136.96±14.99 |
| DBP (mmHg) | 80.46±11.12 | 81.92±11.81 | 83.78±11.29 |
| TG (mmol/L) | 2.03±1.05 | 2.11±1.19 | 2.11±1.11 |
| TC (mmol/L) | 4.76±1.13 | 4.84±1.08 | 4.81±1.12 |
| HDL-C (mmol/L) | 1.12±0.24 | 1.18±0.22 | 1.12±0.24 |
| LDL-C (mmol/L) | 2.93±0.62 | 2.95±0.76 | 2.97±0.84 |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| **Fasting serum insulin (μIU/mL)** | **10.29±4.72** | **11.59±6.45** | **13.27±8.37\*** |
| Estradiol (pg/ml) | 24.54±7.67 | 25.61±7.39 | 24.68±7.41 |
| **HOMA-IR** | **2.21±1.13** | **2.71±1.44** | **3.48±2.26\*#** |
| MetS | n=31 | n=79 | n=40 |
| **Age (years)** | **64.35±5.16** | **63.09±3.72** | **61.85±3.59\*#** |
| **BMI (kg/m2)** | **27.85±3.02** | **24.19±2.83\*** | **25.78±1.42\*#** |
| Waist circumference (cm) | 87.87±5.08 | 88.87±5.86 | 87.35±3.83 |
| FBG (mmol/L) | 6.92±1.09 | 7.02±1.46 | 7.25±1.48 |
| HbA1C (%) | 6.90±0.92 | 6.75±0.84 | 6.57±0.94 |
| **SBP (mmHg)** | **144.81±7.34** | **148.73±6.67\*** | **149.25±6.42\*** |
| DBP (mmHg) | 91.55±4.98 | 92.72±4.46 | 92.73±4.29 |
| TG (mmol/L) | 2.23±0.80 | 2.35±1.11 | 2.53±1.11 |
| TC (mmol/L) | 4.97±0.90 | 5.09±1.05 | 5.05±1.07 |
| **HDL-C (mmol/L)** | **0.90±0.12** | **1.01±0.14\*** | **0.95±0.13** |
| LDL-C (mmol/L) | 3.08±0.62 | 3.03±0.87 | 3.11±0.97 |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| Fasting serum insulin (μIU/mL) | 12.62±4.74 | 14.04±7.10 | 16.01±8.63 |
| Estradiol (pg/ml) | 24.87±9.28 | 22.75±6.37 | 22.80±7.07 |
| **HOMA-IR** | **2.63±1.03** | **3.30±1.50** | **4.39±2.25\*#** |
| Control | n=38 | n=84 | n=32 |
| Age (years) | 62.16±6.37 | 63.06±4.30 | 63.16±3.90 |
| BMI (kg/m2) | 22.99±2.61 | 22.28±3.17 | 22.49±3.01 |
| Waist circumference (cm) | 82.53±2.61 | 81.50±2.07 | 82.28±3.14 |
| FBG (mmol/L) | 4.98±0.81 | 5.26±0.70 | 5.16±0.66 |
| HbA1C (%) | 5.20±0.37 | 5.18±0.37 | 5.34±0.50 |
| SBP (mmHg) | 123.58±3.71 | 121.69±5.22 | 121.59±4.89 |
| DBP (mmHg) | 71.42±4.48 | 71.76±6.17 | 72.59±5.98 |
| TG (mmol/L) | 1.87±1.20 | 1.90±1.23 | 1.59±0.88 |
| TC (mmol/L) | 4.59±1.27 | 4.61±1.06 | 4.51±1.12 |
| HDL-C (mmol/L) | 1.31±0.12 | 1.34±0.14 | 1.34±0.15 |
| LDL-C (mmol/L) | 2.81±0.61 | 2.87±0.64 | 2.79±0.61 |
| NAFLD (%)  | 28 (37.8) | 70 (45.5) | 45 (59.2) |
| Fasting serum insulin (μIU/mL) | 8.40±3.81 | 9.29±4.79 | 9.84±6.70 |
| **Estradiol (pg/ml)** | **24.26±6.16** | **28.30±7.30\*** | **27.03±7.36** |
| HOMA-IR | 1.88±1.11 | 2.16±1.15 | 2.34±1.73 |

Continuous data were presented as mean±SD and analyzed by one-way ANOVA and the Bonferroni method for multiple comparisons between groups.

Categorical data are presented as n (%) and analyzed using chi-square test.

\*P<0.05 vs. the AA group

#P<0.05 vs. the AG group

Abbreviations: FBG, fasting blood glucose; HbA1C, hemoglobin A1C; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, Triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NAFLD, non-alcoholic fatty liver disease; HOMA-IR, homeostasis model assessment of insulin resistance.

**Supplementary Figure S1.** Genotype validation by direct sequencing for PvuII and XbaI.



**Supplementary Figure S2.** Genotype validation by direct sequencing for RsaI.



**Supplementary Figure S3.** Genotype validation by direct sequencing for AluI.

