

Supplementary tables:

Table 1: Genotype distribution and allele frequencies of the Asp358Ala polymorphism of the *IL6R* in subgroups of type 2 diabetic patients and glucose tolerant subjects

| | NGT subjects from the Inter99 cohort | Elderly NGT subjects | T2D patients from the Inter99 cohort | T2D patients from Steno Diabetes Center |
|----------------------|--------------------------------------|----------------------|--------------------------------------|---|
| N (M/W) | 4251 (1972/2279) | 345 (164/181) | 324 (202/122) | 1025 (617/408) |
| Asp/Asp | 1495 (35.2%) | 117 (33.9%) | 123 (38.0%) | 386 (37.7%) |
| Asp/Ala | 2013 (47.4%) | 167 (48.4%) | 158 (48.8%) | 489 (47.7%) |
| Ala/Ala | 743 (17.5%) | 61 (17.7%) | 43 (13.3%) | 150 (14.6%) |
| Ala allele % (95%CI) | 41.2 (40.1-42.2) | 41.9 (38.2-45.6) | 37.7 (33.9-41.4) | 38.5 (36.3-40.6) |

Data are number of subjects with each genotype (% of each group). T2D denotes diabetes mellitus. NGT denotes glucose tolerant. M denotes men and W denotes women.

The genotype distributions and the allele frequencies of the Asp358Ala polymorphism of the *IL6R* in the various subgroups were not significantly different within groups of NGT subjects or within groups of type 2 diabetic subjects, respectively. All study participants were recruited from the same area of Copenhagen and all were Danish Whites. Both subgroups of NGT subjects were recruited by random through the Danish Central Population Register and are therefore population based. In a logistic regression analysis including the various study groups as a categorical covariate, we did not find a significant effect of study groups. Consequently, study groups were not included in the final analytical model.

Table 2a: Clinical and biochemical data of 653 middle-aged IGT white subjects when classified in accordance to their genotype of the Asp358Ala polymorphism of *IL6R*

| | Asp/Asp | Asp/Ala | Ala/Ala | <i>p</i> | <i>p</i> <i>recessive</i> | <i>p</i> <i>dominant</i> |
|-------------------------------------|------------------|------------------|------------------|----------|------------------------------|-----------------------------|
| N (M/W) | 234 (114/120) | 304 (147/157) | 115 (59/56) | | | |
| Age (years) | 48 ± 8 | 48 ± 8 | 50 ± 7 | | | |
| BMI (kg/m ²) | 28.2 ± 5.1 | 27.9 ± 5.0 | 28.5 ± 5.6 | NS | NS | NS |
| Waist/Hip ratio | 0.89 ± 0.09 | 0.88 ± 0.09 | 0.89 ± 0.08 | NS | NS | NS |
| P-glucose 0 min (mmol/l) | 5.8 ± 0.5 | 5.7 ± 0.5 | 5.7 ± 0.6 | NS | NS | NS |
| P-glucose 120 min (mmol/l) | 8.9 ± 0.8 | 8.9 ± 0.9 | 8.7 ± 0.7 | NS | NS | NS |
| Incremental AUC-glucose (mmol/l) | 378 ± 87 | 387 ± 93 | 384 ± 90 | NS | NS | NS |
| S-Insulin 0 min (pmol/l) | 54 ± 37 | 56 ± 35 | 51 ± 30 | NS | NS | NS |
| S-Insulin 120 min (pmol/l) | 427 ± 326 | 463 ± 361 | 437 ± 313 | NS | NS | NS |
| Incremental AUC-insulin | 30906 ± 21936 | 33970 ± 25446 | 32569 ± 21665 | NS | NS | NS |
| Insulinogenic index-insulin | 24.7 ± 18.2 | 26.5 ± 19.3 | 26.2 ± 19.0 | NS | NS | NS |
| HOMA-IR | 13.9 ± 9.8 | 14.4 ± 9.5 | 13.1 ± 8.2 | NS | NS | NS |
| S-Cholesterol (mmol/l) | 5.7 ± 1.1 | 5.8 ± 1.2 | 5.8 ± 1.1 | NS | NS | NS |
| S-HDL Cholesterol (mmol/l) | 1.36 ± 0.37 | 1.40 ± 0.45 | 1.39 ± 0.42 | NS | NS | NS |
| S-Triglycerides (mmol/l) | 1.64 ± 0.98 | 1.90 ± 3.68 | 1.64 ± 0.91 | NS | NS | NS |

Data are presented as mean (± SD). *p*-values comparing “Asp/Asp, Asp/Ala and Ala/Ala” *p*_{rec}

comparing “Asp/Asp and Asp/Ala” to “Ala/Ala” were obtained after adjustment for age, BMI and

gender. AUC; area under the curve, HOMA-IR; homeostasis model assessment-insulin resistance index, p; plasma and s; serum. NS; not significant. M. denotes men and W. denotes women.

Table 2b: Clinical and biochemical data of 474 middle-aged IFG white subjects when classified in accordance to their genotype of the Asp358Ala polymorphism of *IL6R*

| | Asp/Asp | Asp/Ala | Ala/Ala | <i>p</i> | <i>p</i> <i>recessive</i> | <i>p</i> <i>dominant</i> |
|-------------------------------------|------------------|------------------|------------------|-----------------|--------------------------------------|-------------------------------------|
| N (M/W) | 170 (125/45) | 219 (163/56) | 85 (63/22) | | | |
| Age (years) | 49 ± 7 | 49 ± 7 | 49 ± 6 | | | |
| BMI (kg/m ²) | 28.0 ± 4.1 | 27.9 ± 5.0 | 28.0 ± 4.5 | NS | NS | NS |
| Waist/Hip ratio | 0.91 ± 0.07 | 0.90 ± 0.08 | 0.90 ± 0.08 | NS | NS | NS |
| P-glucose 0 min (mmol/l) | 6.3 ± 0.2 | 6.4 ± 0.2 | 6.3 ± 0.2 | NS | NS | NS |
| P-glucose 120 min (mmol/l) | 6.0 ± 1.0 | 5.9 ± 1.2 | 5.8 ± 1.2 | NS | NS | NS |
| Incremental AUC-glucose (mmol/l) | 229 ± 93 | 217 ± 104 | 221 ± 97 | NS | NS | NS |
| HbA1c% | 6.0 ± 0.4 | 6.0 ± 0.4 | 6.0 ± 0.4 | NS | NS | NS |
| S-Insulin 0 min (pmol/l) | 51 ± 28 | 51 ± 29 | 49 ± 28 | NS | NS | NS |
| S-Insulin 120 min (pmol/l) | 216 ± 174 | 203 ± 156 | 205 ± 165 | NS | NS | NS |
| Incremental AUC-insulin | 24472 ± 16432 | 22609 ± 13667 | 24495 ± 16280 | NS | NS | NS |
| Insulinogenic index-insulin | 27.0 ± 19.0 | 25.8 ± 17.1 | 28.5 ± 20.9 | NS | NS | NS |
| HOMA-IR | 14.2 ± 7.9 | 14.4 ± 8.1 | 13.7 ± 8.1 | NS | NS | NS |
| S-Cholesterol (mmol/l) | 5.8 ± 1.1 | 6.0 ± 1.1 | 6.0 ± 1.0 | NS | NS | NS |
| S-HDL Cholesterol (mmol/l) | 1.41 ± 0.40 | 1.37 ± 0.42 | 1.35 ± 0.36 | NS | NS | NS |
| S-Triglycerides (mmol/l) | 1.41 ± 0.40 | 1.37 ± 0.42 | 1.35 ± 0.36 | NS | NS | NS |

Data are presented as mean (± SD).). *p*-values comparing “Asp/Asp, Asp/Ala, Ala/Ala” *p* *recessive*

comparing “Asp/Asp and Asp/Ala” to “Ala/Ala”, and *p* *dominant* comparing “Asp/Asp” to “Asp/Ala and Ala/Ala” were obtained after adjustment for age, BMI and gender. AUC; area under the curve, HOMA-IR; homeostasis model assessment-insulin resistance index, p; plasma and s; serum. NS; not significant. M. denotes men and W. denotes women.