DGI: Insulinogenic Index Trait Document

Calculation:
\[
\frac{\text{Insulin}_{30} - \text{Insulin}_0}{\text{Glucose}_{30} - \text{Glucose}_0}
\]
Units: insulin in µU/ml and fasting plasma glucose in mmol/L

Measurement:
Insulin (µU/ml) measured using radioimmunoassay kits:
1) Pharmacia
2) DAKO insulin
3) Delfia
Plasma glucose (mmol/L) measured by a glucose oxidase method
1) Fasting blood glucose from venous blood (B-Gluc) and converted to plasma glucose value (correction factor 1.13)
2) Plasma from venous blood using Beckman or Hemocue Glucose Analyzers
3) Plasma from capillary blood using a Hemocue Glucose Analyzer

Trait Distribution:

<table>
<thead>
<tr>
<th>Sample</th>
<th>n</th>
<th>Mean (mU/mmol)</th>
<th>SD (mU/mmol)</th>
<th>Median (mU/mmol)</th>
<th>IQR (mU/mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-diabetes controls</td>
<td>1119</td>
<td>22.6</td>
<td>29.4</td>
<td>15.8</td>
<td>16.6</td>
</tr>
<tr>
<td>Males</td>
<td>536</td>
<td>19.9</td>
<td>23.3</td>
<td>14.8</td>
<td>14.6</td>
</tr>
<tr>
<td>Females</td>
<td>583</td>
<td>25.1</td>
<td>33.8</td>
<td>16.8</td>
<td>16.1</td>
</tr>
</tbody>
</table>

SD=standard deviation, IQR=interquartile range

Raw insulinogenic index values
Description of Trait Modeling:
Insulinogenic index was logarithmically transformed to fit a normal distribution. Z scores were prepared separately by gender and recruiting region (Botnia, Skara, Malmo or Helsinki) and regressed against age, log BMI and type of insulin measurement.

Covariates:
Gender, recruiting region, age, log BMI, type of insulin measurement

Correlation among related quantitative traits:

Pearson correlations:
- Ins Index and HOMA-IR: 0.29
- Ins Index and Fasting Plasma Glucose: 0.03
- Ins Index and TG/HDL ratio*: 0.15

* TG/HDL ratio in controls is used as a measure of insulin resistance

Counts of individuals used to generate results on Web-site:

<table>
<thead>
<tr>
<th>Trait</th>
<th>Analysis sample</th>
<th>Unaffected</th>
<th>T2D Affected</th>
<th>Total analyzed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sibs</td>
<td>UNR</td>
<td>Total</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulinogenic index</td>
<td>controls only</td>
<td>113</td>
<td>895</td>
<td>1008</td>
</tr>
</tbody>
</table>

Summary of association testing method:
Linear regression was used to test the association between SNP genotype and insulinogenic index z-score. Unrelated individuals and siblings were included in this analysis. P values are reported after correction by genomic control. Genomic inflation factor (based on the median chi-squared) was 1.05.

Additional Comments: