Background

• Individuals with type 2 diabetes (T2D) are at a greater risk of developing cardiovascular disease (CVD).

A genome-wide association study (GWAS) of individuals of varying ancestry diagnosed with T2D was conducted, which is uncommon in a developing cardiovascular disease (CVD).

For rs147138607 and rs335407, the literature ancestry diagnosed with T2D in patients with T2D in each novel region.

• Ancestry-specific Z-scores and ancestry-specific pairwise linkage disequilibrium were run in fine mapping software MSCAVAR.

• For rs147138607 and rs335407 regions, the 95% credible sets included 21 and 38 variants, respectively.

• These results will help prioritize likely causal variants for functional follow-up.

• Future fine-mapping work will include incorporating functional annotations, as well as running ancestry-specific analyses.

Results

rs147138607 P-Values in Meta Analysis

<table>
<thead>
<tr>
<th>Variant ID</th>
<th>P-value</th>
<th>Z-Score</th>
<th>Causal Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:181856462:C-G</td>
<td>3.8×10^-9</td>
<td>7.9</td>
<td>0.17</td>
</tr>
<tr>
<td>rs147138607</td>
<td>1:18185116:TC</td>
<td>6.5×10^-8</td>
<td>5.8</td>
</tr>
<tr>
<td>rs181839668:DI</td>
<td>8.3×10^-8</td>
<td>-5.8</td>
<td>0.10</td>
</tr>
<tr>
<td>rs181843728:D-I</td>
<td>1.5×10^-7</td>
<td>-9.7</td>
<td>0.08</td>
</tr>
<tr>
<td>rs18185077:TC:TC</td>
<td>1.4×10^-6</td>
<td>5.7</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Figure 1: Regional Plot of rs147138607 Region after Fine Mapping Genetic Loci showing Novel Associations with Incident Cardiovascular Disease in Type 2 Diabetes

Conclusion

• Both regions had relatively large 95% credible sets

• Region containing rs147138607 had 21 variants

• Region containing rs335407 had 38 variants

• Smaller credible sets of 2-3 variants are favorable due to high cost of laboratory follow-up

• Large credible set size likely due to limitations of analysis, including

• Exclusion of variants not present in all ancestries (in GWAS results)

• Exclusion of variants with more than 2 alleles

• Relatively small sample size

• Future work will attempt to address limitations by

• Conducting ancestry-specific analyses – less variants excluded

• Incorporating functional annotations – further reduce credible set

References


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