Case-Control Association Analysis of Four SNPs with Atrial Fibrillation

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Hypothesis

- Atrial Fibrillation, or AF, is the most common form of irregular heart beat with Familial Atrial Fibrillation making up nearly 30% of all AF cases.
- This suggests that a genetic variant is a potential risk factor of the disease.
- We recently have conducted one GWAS for AF in Chinese Han Population and identified 8 significant SNPs.
- Since GWAS relies heavily on large replication studies and studies for AF had only been done for the Chinese Han population, we planned to apply Taqman Assay to evaluate the association of the 8 SNPs with AF across 624 AF patients and 560 controls at CCF.
- We hypothesized that the eight GWAS risk variants identified from Chinese populations may also confer risk to AF in other populations.

Methodology

- 5μL PCR reaction Mix:
  - 2x Taqman Master Mix
  - 40x Taqman Assay
  - DNA templates and water
- Dual 384-well PE 9700 systems
- Taqman Genotyping was done to analyze the genotype of the case and control samples.
- By running tests comparing the occurrence of each SNP in these samples, we determined the significance of our data.
- Statistical Analysis:
  - Hardy-Weinberg Equilibrium Test
  - Allelic association, 2 by 2 Chi-squared test
  - Genotypic analysis under 3 genetic models
  - PLINK was used to run these tests.

Results

- Results of Genotypic Association of 4 SNPs with AF

<table>
<thead>
<tr>
<th>SNP ID</th>
<th>Model</th>
<th>Case</th>
<th>Control</th>
<th>OR (95%CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs3804987</td>
<td>Additive</td>
<td>19/33/313</td>
<td>13/191/356</td>
<td>1.04</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>Dominant</td>
<td>151/313</td>
<td>204/356</td>
<td>1.32</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>Reccessive</td>
<td>19/445</td>
<td>13/547</td>
<td>1.06</td>
<td>0.20</td>
</tr>
<tr>
<td>rs17255683</td>
<td>Additive</td>
<td>67/255/261</td>
<td>53/256/247</td>
<td>0.93</td>
<td>0.34</td>
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<tr>
<td></td>
<td>Dominant</td>
<td>322/261</td>
<td>309/247</td>
<td>1.11</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td>Reccessive</td>
<td>67/516</td>
<td>53/503</td>
<td>0.57</td>
<td>0.28</td>
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<tr>
<td>rs2200733</td>
<td>Additive</td>
<td>56/227/332</td>
<td>11/167/377</td>
<td>1.00</td>
<td>0.17</td>
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<tr>
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<td>Dominant</td>
<td>283/332</td>
<td>178/377</td>
<td>1.00</td>
<td>0.67</td>
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<tr>
<td></td>
<td>Recressive</td>
<td>56/559</td>
<td>11/544</td>
<td>1.00</td>
<td>0.59</td>
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<tr>
<td>rs10499312</td>
<td>Additive</td>
<td>0/49/565</td>
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<td>0.01</td>
<td>0.93</td>
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<tr>
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<td>33/521</td>
<td>1.00</td>
<td>0.62</td>
</tr>
<tr>
<td></td>
<td>Recressive</td>
<td>0/614</td>
<td>0/554</td>
<td>0.01</td>
<td>0.93</td>
</tr>
</tbody>
</table>

SNP rs2200733 showed a statistically significant P-value (1.16 × 10⁻⁵) as well as a high OR value (1.85) signifying confidence in the data in our Allelic Association test.

- Once again, SNP rs2200733 showed up as statistically significant in its association to AF in Additive, Dominant, and Recessive association test results.

Conclusions

- We found the SNP rs2200733 was statistically significant with AF in CCF AF cohort, with OR of 1.85. This positive association was consistent with published GWAS.
- The other 3 SNPs did not demonstrate statistical evidence for association with AF. Their effects were relatively low (OR of 1.08-1.35), indicating larger samples are needed to confirm results.

Recommendations

- In the future, we will further analyze these negative associations in larger samples to confirm such associations. We also analyze more SNPs with suggestive significant level. Identification of new AF risk variants is the key to understanding the genetic basis of AF.

References