Transcription Factor PITX3 Gene in Parkinson’s Disease

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Abstract

PITX3 is a transcription factor important for the differentiation and survival of midbrain dopaminergic neurons during the development. Single nucleotide polymorphisms (SNP) in the gene may be associated with Parkinson’s Disease (PD). To verify their findings and to determine the nature of the association in a subset of our PD patients we have analyzed two PITX3 SNPs (rs2281983 and rs4919621) in PD patients and age-matched health controls. Our data show that the substitutions of C/T in SNP1 and A/T in SNP2 are significantly higher in PD, and this finding is even more robust in young onset and familial PD as compared with age-matched healthy controls. Our findings indicate that PITX3 may play a role in the pathogenesis of PD.

Results

1. The frequency of substitutions of C/T in SNP1 rs2281983 and A/T in SNP2 rs4919621 is significantly higher in PD, and it is particularly high in EOPD and IPD as compared with age-matched healthy controls.

2. Our results support the hypothesis that PITX3 is critical not only in the development and maintenance of the dopaminergic system, but also in the pathogenesis of PD.

Conclusions

Patients: 265 North American Caucasian PD patients and 210 healthy controls from the Parkinson’s Disease Center and Movement Disorders Clinic (PDCMDC), Baylor College of Medicine (BCM). All research subjects signed an informed consent, approved by BCM institutional Review Board for Human Research. PD samples were subcategorized into EOPD, LOPD, familial PD and sporadic PD.

Material and Methods

PCR: Genomic DNA was extracted from peripheral blood using standard protocols. PCR products of PITX3 were amplified with the following primers:

<table>
<thead>
<tr>
<th>Allele</th>
<th>Controls</th>
<th>Total PD</th>
<th>EOPD</th>
<th>LOPD</th>
<th>IPD</th>
<th>sPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs2281983</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>T</td>
<td>248 (0.529)</td>
<td>271 (0.533)</td>
<td>78 (0.481)</td>
<td>193 (0.556)</td>
<td>89 (0.454)</td>
<td>132 (0.545)</td>
</tr>
<tr>
<td>C</td>
<td>172 (0.471)</td>
<td>258 (0.469)</td>
<td>84 (0.519)</td>
<td>175 (0.444)</td>
<td>187 (0.546)</td>
<td>152 (0.455)</td>
</tr>
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</table>

Empirical-P

Adjusted OR (95%CI)

Acknowledgement

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References