Heme oxygenase-1 gene promoter polymorphism and decline in lung function in Japanese men

Chronic obstructive pulmonary disease (COPD) is characterised by progressive airflow limitation in the lung airway. Cigarette smoking is the most important risk factor for COPD. Heme oxygenase-1 (HO-1) is a key enzyme in the body that regulates the protective response against oxidative stress. A (GT)n dinucleotide repeat in the human HO-1 promoter shows length polymorphism which is characterised into three groups: S-allele (<27 GT repeats), M-allele (27–32 GT repeats), and L-allele (>33 GT repeats). The L-allele was found to be associated with reduced HO-1 inducibility and susceptibility to pulmonary epithelial cell death in a case-control study of Japanese male smokers. Conversely, Ho et al. reported that HO-1 polymorphism was not related to a rapid decline in lung function in a prospective study of white smokers.

To evaluate the role of HO-1 polymorphism in the decline in lung function in Japanese subjects, 101 Japanese male ex-smokers with mild to severe COPD (forced expiratory volume in 1 second (FEV1) ≤ 40–90% predicted and FEV1/FVC < 70%) were enrolled from January 2000 to December 2001 and HO-1 polymorphism was checked by PCR with peripheral blood DNA. Spirometric tests were performed at the beginning of the study and annually for 3 years. Smoking status, baseline FEV1 predicted, and L-allele carrier status. As a result, the adjusted odds ratio of L-allele carrier status for rapid decliners was 3.9 (95% CI 1.4 to 10.6), p = 0.009 (12 (48.9%) in L-allele carriers) and 13 (17.8%) in non-L-allele carriers (12 (42.9%) v 13 (17.8%), p = 0.009, \( x^2 \) test, table 1). Furthermore, the factors associated with a rapid decline in lung function were calculated by multivariate logistic regression analysis to adjust for potential risk factors including age, smoking status (pack-years), baseline FEV1, predicted, and L-allele carrier status. As a result, the mean annual decline in FEV1 predicted in L-allele carriers was significantly larger than in non-carriers (mean (SE) 2.74 (1.22)% per year v –0.57 (0.89)% per year, \( \beta = 0.044 \), unpaired \( t \) test, table 1).

### Table 1 Mean (SE) baseline characteristics and decline in lung function in L-allele carriers and non-L-allele carriers

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>L-allele carrier (n = 28)</th>
<th>Non-L-allele carrier (n = 73)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.3 (1.7)</td>
<td>70.6 (0.9)</td>
<td>0.84***</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>28/0</td>
<td>73/0</td>
<td>&gt;0.99**</td>
</tr>
<tr>
<td>Smoking status</td>
<td>28 (100%)</td>
<td>73 (100%)</td>
<td>&gt;0.99**</td>
</tr>
<tr>
<td>No of ex-smokers</td>
<td>72 (100%)</td>
<td>73 (100%)</td>
<td>&gt;0.99**</td>
</tr>
<tr>
<td>Pack-years</td>
<td>44.7 (4.6)</td>
<td>49.3 (3.6)</td>
<td>0.47***</td>
</tr>
</tbody>
</table>

All subjects had a smoking history of at least 10 pack-years and had quit smoking at least 6 months before the study. Lung function was assessed at bronchodilator and spirometry.

*Unpaired \( t \) test; **Fisher’s exact test; *** \( x^2 \) test.

† Rapid decline is defined as a mean annual decrease in FEV1 > 3.0% predicted.

### References


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