Common mutations in Cuban cystic fibrosis patients

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Abstract

So far, more than 1500 mutations have been reported in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Mutational spectrum varies in accordance with geographic and/or ethnic origin. In this study, we have analyzed seven common CF mutations (p.F508del, p.G542X, p.R1162X, p.N1303K, p.R334W, p.R553X and c.3120+1G>A) taking into account the ethnic origin of the Cuban population which is mainly influenced by Spanish and sub-Saharan African contribution. All but p.N1303K have been detected in our patients, the p.F508del being the most prevalent (37.9%). Overall, six mutations showed frequencies above 1% accounting for 55.5% of the Cuban CF alleles.

Keywords: Cystic fibrosis; CFTR gene; Cuban population

1. Introduction

In a previous study, the CF incidence in the Cuban population has been estimated 1/5000 [1]. Taking into account the Spanish and sub-Saharan African contribution to our population which represent 60% and 40%, respectively [2], we have considered starting the study in our patients analyzing the most common CF mutations in those populations [3,4]. The aim of this work is the molecular characterization of the Cuban CF population that will allow us to confirm the clinical diagnosis and provide more reliable genetic counselling to the patients and their families.

2. Materials and methods

2.1. Patients

The CF unrelated patients (n=153) were diagnosed by clinical characteristics of the disease and positive sweat test (≥60 mmol/L) [5]. In addition, the diagnoses were approved by the CF National Commission. The study was approved by the local Ethics Committee and informed written consent was obtained from all participants or their parents.

Table 1

Frequencies of cystic fibrosis mutations in the Cuban population (n=153)

<table>
<thead>
<tr>
<th>Mutation</th>
<th>CF alleles</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>p.F508del</td>
<td>116</td>
<td>37.9</td>
<td></td>
</tr>
<tr>
<td>p.G542X</td>
<td>21</td>
<td>6.8</td>
<td></td>
</tr>
<tr>
<td>p.R334W</td>
<td>16</td>
<td>5.2</td>
<td></td>
</tr>
<tr>
<td>p.R553X</td>
<td>7</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>p.R1162X</td>
<td>6</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>c.3120+1G&gt;A</td>
<td>4</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>p.N1303K</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>170</td>
<td>55.5</td>
<td></td>
</tr>
</tbody>
</table>

ª Newton et al. [6].
ª Gasparini et al. [7].
ª Cutting et al. [8].
ª Zielenski et al. [9].
2.2. Analysis of common mutations


3. Results and discussion

CF mutational spectrum has been observed specific for different populations [10]. The present Cuban population is the result of a mixing contribution from Spanish and sub-Sahara African populations. Taking into account this ethnic origin we have performed direct analysis of seven common CF mutations. We have identified six out of seven mutations accounting for 55.5% of the CF alleles. All six mutations showed frequencies above 1% indicating enough efficiency from our preliminary strategy considering the ethnic composition in Cuba (Table 1).

In contrast with our previous data [11] a lower frequency for p.F508del mutation (37.9%) was found, this discrepancy could be likely due to clinical criteria inclusion followed here. However, the present estimated prevalence is similar to other Latin American countries (Table 2) [3,12]. Concerning the frequency of p.G542X mutation (6.8%), a high prevalence of this mutation has also been reported in Mexico (6.2%) [14] and Costa Rica (25%) [18], strongly suggesting the Spanish influence in all cases. Such founder effect could also be postulated for p.R334W mutation (5.2% in Cuba).

As expected regarding our African ancestry the c.3120+1G>A mutation was found in 1.3% of the CF alleles. The higher frequency of this mutation in Latin America has been reported in Brazil (Table 2) [17]. This CF variable spectrum in Latin American countries has been recently reviewed by Pérez et al. [19]. The present work represents the major contribution to the molecular profile of CF in Cuban population with six mutations accounting for 55.5% of alleles, which will allow us to design one specific diagnostic panel for CF mutations. Furthermore, our results will contribute to improve the genetic counselling for the patients and their relatives. Nowadays, we are performing an extensive CFTR gene analysis to accurately define the specific molecular profile of CF in Cuba.

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References


