Two novel mutations in the β-myosin heavy chain gene associated with dilated cardiomyopathy


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Abstract

Background: Dilated cardiomyopathy (DCM) is familial in approximately 20–35% of cases of idiopathic DCM. Several mutations in the different sarcomere protein genes have been reported to cause DCM. Aims: We wanted to investigate the role of sarcomere protein gene variants in Finnish DCM patients. Methods and results: We screened all coding exons of five sarcomere protein genes (β-myosin heavy chain, α-tropomyosin, troponin C, troponin I and troponin T) in a well-characterized population of 52 DCM patients in Eastern Finland by the PCR-SSCP and sequencing method. Two novel mutations, Arg1053Gln and Arg1500Trp, in the β-myosin heavy chain gene in two index patients were detected. The proband with the Arg1053Gln mutation had a dilated left ventricle and impaired systolic function, but other family members carrying this mutation presented with septal hypertrophy. It thus seems that the Arg1053Gln mutation is primarily a HCM mutation, which can also lead to DCM. The other mutation, Arg1500Trp, was associated with a typical DCM phenotype. The Arg1500Trp mutation carrier had only one family member alive, but she did not carry the mutation and, therefore, cosegregation of the mutation and the disease in this family could not be reliably verified. No disease-causing mutations were found in the other sarcomere protein genes. Conclusions: Two novel mutations in the β-myosin heavy chain gene were detected in patients with DCM. Overall, mutations in the β-myosin heavy chain gene seem to be relatively uncommon in Finnish DCM patients.

Keywords: Dilated; Hypertrophy cardiomyopathy; Sarcomere protein gene

1. Introduction

Dilated cardiomyopathy (DCM) is a heterogeneous disease having variable etiological and clinical features. DCM is familial in approximately 20–35% of cases of idiopathic DCM, but the genetic basis of this disease is largely unknown [1,2]. To date, the disease-associated gene defects have been reported in 16 different genes [3–17]. Over 10 DCM-associated mutations have been reported in eight different sarcomere protein genes including cardiac actin, α-tropomyosin, β-myosin heavy chain, troponin T, myosin-binding protein-C, titin, telethonin and troponin I genes [3,7,10,11,14,16–19]. The DCM-causing mechanisms have been classified into four main groups: in the first group force generation, in the second group force transmission, in the third group energy production are affected and in the last group the disease-causing mechanisms remain unclear [20].

Over 150 mutations in 11 sarcomere protein genes have been reported to be associated with hypertrophic cardiomyopathy (HCM) [21–23]. Primarily, HCM patients have normal systolic function and no dilatation of the left ventricle. However, a small proportion (~10%) of HCM patients develop heart failure with dilatation of left ventricle and reduced ejection fraction, the phenotype resembling that of DCM [24]. Several clinical reports of transition from HCM to DCM have been published [25–27], but only a few specific mutations associated with the transition forms of HCM have been described to date. Mutations in the troponin T, α-tropomyosin, β-myosin heavy chain, and myosin binding...
protein-C genes, but also in the mitochondrial genome (mtDNA), are known to be associated with a transition from HCM-type disease to DCM-type disease [28–35]. Mutations in the mtDNA, e.g., 3243A>G, usually cause HCM, but also primary DCM has been encountered [36].

Although several mutations in the sarcomere protein genes in DCM have been reported, they explain the disease only in isolated families. Previously, we have already screened the cardiac actin gene in our DCM study group, but did not find any disease-associated variants [37]. To investigate further whether defects in other sarcomere protein genes would cause DCM in Finnish patients, we screened the entire coding regions of the β-myosin heavy chain, α-tropomyosin, cardiac troponin C, I and T genes.

2. Methods

2.1. Subjects and clinical evaluation

We studied 52 DCM patients from the Kuopio University Hospital region in Eastern Finland. Eight index patients were classified as familial and 44 index patients as sporadic cases. The diagnostic criteria for DCM were left ventricular ejection fraction < 45% and left ventricular end-diastolic diameter > 27 mm/m² in the absence of secondary causes for DCM [38]. The diagnostic criteria for HCM were left ventricular wall thickness ≥ 15 mm, blood pressure ≤ 160/100 mm Hg, and no other causes for ventricular hypertrophy (e.g., primary valvular disease). The patients were evaluated by personal and family history, physical examination, 12-lead electrocardiography (ECG), chest X-ray and transthoracic echocardiography (M-mode, two-dimensional and Doppler). Furthermore, 87% of patients with DCM underwent diagnostic coronary angiography. All available first-degree relatives of the eight families were evaluated by physical examination, 12-lead ECG and transthoracic echocardiography. The diagnostic criteria for family members were the same as previously described [39]. The study protocol was approved by the Ethics Committees of the University of Kuopio and University of Helsinki, and it was in accordance with the Helsinki Declaration.

The study group consisted of 37 men and 15 women, and the mean age at the time of diagnosis was 50 years (range, 11 to 71 years). Left ventricular end-diastolic diameter (LVEDD) varied from 51 to 99 mm (mean 65 mm) and the mean ejection fraction was 34%.

2.2. Additional study group

We screened an additional group of 104 DCM patients for the two mutations (which were found in this study in exons 25 and 32) in the β-myosin heavy chain gene. In this additional study group there were 15 subjects with confirmed familial disease, and the rest of the group was determined to represent sporadic cases. The majority of patients in this additional study group (n = 66) underwent heart transplantation, the others living in the area of Helsinki University Hospital.

2.3. Controls

One hundred fifty clinically healthy control subjects without any family history of DCM formed the control group. Echocardiography was performed on 82 of these control subjects and it did not reveal any findings suggesting cardiomyopathy. Control subjects were screened by PCR-SSCP method.

2.4. Laboratory methods

Genomic DNA extraction and the details of the polymerase chain reaction (PCR) and single-strand conformation polymorphism analysis (SSCP) have been described [37]. Our SSCP method has been previously validated against the known variants of the lipoprotein lipase gene [40,41]. Primers for the β-myosin heavy chain, troponin C, I and T genes were designed according to the Genbank sequences M57965, M37984, X90780 and AY044273, respectively, and primers for the α-tropomyosin gene were synthesized as previously reported [42]. The PCR conditions were denatured at 94 °C for 3 min, followed by 35 cycles of denaturation at 94 °C for 40 s, annealing at 56–68 °C for 20–45 s and extension at 72 °C for 30–60 s with final extension at 72 °C for 4 min.

Genomic DNA from individuals with variant SSCP patterns was sequenced with ABI Prism BigDye Terminator Cycle Sequencing Ready Reaction Kits using ABI Prism 310 Genetic Analyzer (Applied Biosystems, Foster City, CA, USA).

3. Results

3.1. Variants in the β-myosin heavy chain gene

All 38 coding exons of the β-myosin heavy chain gene were screened with the PCR-SSCP method for variants. We detected two formerly unreported mutations, Arg1053Gln and Arg1500Trp, in the β-myosin heavy chain gene in two Finnish patients with DCM (Figs. 1 and 2). The Arg1053Gln mutation showed cosegregation with the clinical disease (Fig. 1 and Table 2). The Arg1500Trp mutation was detected only in one DCM patient, and her healthy offspring did not carry the mutation. The deceased mother of the index patient with the Arg1500Trp mutation suffered heart failure and cardiomegaly was detected in her chest X-ray, however. Because DNA sample was not available the presence of the mutation could not be verified. Additionally, none of these mutations was found in 150 healthy control subjects nor in the additional study group of DCM patients (n = 104), excluding the possibility of common polymorphism. Several other variants were also found...
in the β-myosin heavy chain among the 52 DCM patients, but all these variants were silent nucleotide substitutions and almost all have also been previously reported. The variants in the β-myosin heavy chain are listed in Table 1.
Table 1
Variants of the β-tropomyosin gene (TNNC1), troponin T gene (TNNT2), and troponin I gene (TNNI3) in 52 DCM patients.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Exon</th>
<th>Mutation/Amino acid change</th>
<th>Controls</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>MYH7</td>
<td>3</td>
<td>Thr63Thr (ACC-ACCT)</td>
<td>Y</td>
<td>[3, 44]</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Phe244Phe (TTT-TTTC)</td>
<td>Y</td>
<td>[3, 44]</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>Gly354Gly (AAG-AAAA)</td>
<td>Y</td>
<td>[3]</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>Lys365Lys (GGG-GGC)</td>
<td>Y</td>
<td>[3]</td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>Thr767Thr (AC1-AC1A)</td>
<td>Y</td>
<td>[44]</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>Ile898Ile (AT-TAC)</td>
<td>Y</td>
<td>[44]</td>
</tr>
<tr>
<td>Exon 25</td>
<td>Arg1053Gln (C-C-C-A-C)</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exon 31</td>
<td>Ser1412Ser (TCT-TCT)</td>
<td>Y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exon 32</td>
<td>Arg1500Trp (C-C-C-G-A-A-G)</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exon 32</td>
<td>Ala1702Ala (GGA-GCA)</td>
<td>Y</td>
<td>[3]</td>
<td></td>
</tr>
<tr>
<td>Exon 33</td>
<td>Thr1522Thr (AC-T-AC1C)</td>
<td>Y</td>
<td>[45]</td>
<td></td>
</tr>
<tr>
<td>Exon 34</td>
<td>Asp1602Asp (GAG-GTA)</td>
<td>Y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exon 35</td>
<td>Ala1702Ala (GGA-GCA)</td>
<td>Y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNP1</td>
<td>4</td>
<td>Ile151Ala (GGC-GCA)</td>
<td>Y</td>
<td>[3]</td>
</tr>
<tr>
<td>Exon 4</td>
<td>Tyr162Tyr (TAT-TAC)</td>
<td>Y</td>
<td>[3]</td>
<td></td>
</tr>
<tr>
<td>Exon 6</td>
<td>UT + 83 bp α → C</td>
<td>Y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exon 5</td>
<td>Arg68Arg (CCG-CGT)</td>
<td>Y</td>
<td>[50]</td>
<td></td>
</tr>
<tr>
<td>Exon 9</td>
<td>Ser79Ser (TC-TCA)</td>
<td>Y</td>
<td>[43, 51]</td>
<td></td>
</tr>
<tr>
<td>Intron</td>
<td>G → T/A</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 – 50 bp</td>
<td>Ile116Ile (ATC-ATT)</td>
<td>Y</td>
<td>[42, 43, 51]</td>
<td></td>
</tr>
<tr>
<td>Exon 15</td>
<td>Lys263Arg (AAG-AAG)</td>
<td>Y</td>
<td>[43]</td>
<td></td>
</tr>
</tbody>
</table>

MYH7, β-tropomyosin heavy chain gene; TNNC1, troponin C gene; TNNT2, troponin I gene; TNNI3, troponin T gene; TPM1, α-tropomyosin gene; N, variant was not found in control subjects; Y, variant was found also in control subjects. Mutations are indicated in bold and changed bases are underlined.

3.2. Patients with the Arg1053Gln mutation in the β-tropomyosin heavy chain gene

The family with the Arg1053Gln mutation presented with two different phenotypes of cardiomyopathy. The clinical characteristics of the family with the Arg1053Gln mutation are presented in Table 2. One of the family members (II: 2) was clinically examined at the age of 14 years. Cardiomegaly in the chest X-ray (530 cm3/m2) and ventricular posterior wall diameter; LVH, left ventricular hypertrophy (according to the criteria of Sokolow. S(V1)+R(V5-V6)>3.5 mV); R1053Q, substitution of arginine to glutamine in codon 1053; SCD, sudden cardiac death.

### Table 2
Characteristics of the disease in the Arg1053Gln mutation

<table>
<thead>
<tr>
<th>Family member</th>
<th>R1053Q mutation</th>
<th>Age at the time of first symptoms (years)</th>
<th>Age at the time of HCM/cardioangiopathy diagnosis (years)</th>
<th>Age at the time of DCM diagnosis (years)</th>
<th>LVEDD (mm) change</th>
<th>EF (%) change</th>
<th>IVSD (mm) change</th>
<th>LVPWD (mm) change</th>
<th>LVH on ECG</th>
<th>CHF</th>
<th>SCD</th>
<th>At the end of follow-up (A = alive, D = dead)</th>
</tr>
</thead>
<tbody>
<tr>
<td>II: 2</td>
<td>yes</td>
<td>36</td>
<td>14</td>
<td>44</td>
<td>−68</td>
<td>70–41</td>
<td>12–13</td>
<td>10–13</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>D 48 years</td>
</tr>
<tr>
<td>II: 3</td>
<td>yes</td>
<td>36</td>
<td>51</td>
<td>–</td>
<td>49–50</td>
<td>72–71</td>
<td>11–17</td>
<td>10–15–11</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>A 54 years</td>
</tr>
<tr>
<td>II: 5</td>
<td>yes</td>
<td>45</td>
<td>45</td>
<td>–</td>
<td>42–38</td>
<td>&gt;50–&gt;50</td>
<td>17–22</td>
<td>12–12</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>A 52 years</td>
</tr>
<tr>
<td>III: 1</td>
<td>yes</td>
<td>26</td>
<td>26</td>
<td>–</td>
<td>39</td>
<td>72</td>
<td>15</td>
<td>9</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>A 26 years</td>
</tr>
<tr>
<td>III: 2</td>
<td>no</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>45</td>
<td>68</td>
<td>11</td>
<td>8</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>A 22 years</td>
</tr>
<tr>
<td>III: 3</td>
<td>no</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>39</td>
<td>60</td>
<td>10</td>
<td>10</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>A 34 years</td>
</tr>
<tr>
<td>III: 5</td>
<td>yes</td>
<td>22</td>
<td>–</td>
<td>–</td>
<td>51</td>
<td>57</td>
<td>16</td>
<td>12</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>A 22 years</td>
</tr>
<tr>
<td>III: 6</td>
<td>yes</td>
<td>30</td>
<td>–</td>
<td>–</td>
<td>49</td>
<td>72</td>
<td>18</td>
<td>11</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
<td>A 30 years</td>
</tr>
<tr>
<td>III: 7</td>
<td>?</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>39</td>
<td>60</td>
<td>10</td>
<td>10</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>A 23 years</td>
</tr>
</tbody>
</table>

CHF, congestive heart failure; EF, ejection fraction; IVSD, interventricular septal diameter; LVEDD, left ventricular end-diastolic diameter; LVPWD, left ventricular posterior wall diameter; LVH, left ventricular hypertrophy (according to the criteria of Sokolow: S(V1)+R(V5-V6)>3.5 mV); R1053Q, substitution of arginine to glutamine in codon 1053; SCD, sudden cardiac death.
There were no significant stenoses in coronary arteries, but clear myocardial bridging in the left anterior descending coronary artery (LAD) was detected. Echocardiography revealed myocardial hypertrophy (IVS 17 mm) with normal LVEDD (42 mm) and EF (over 50%). After 10 years myocardial hypertrophy had progressed (IVS 22 mm), but there were no signs of left ventricular dilatation or decreased ejection fraction.

All children of the affected family members were clinically examined with the exception of one (III: 4), who had died due to stomach cancer. Three family members of the third generation were clinically and genetically affected. All of them had similar phenotype and findings in echocardiography (LVH on ECG and IVSds of 15/16/18 mm). None of them had ventricular dilatation, and EF was normal. One family member (III: 7) had normal ECG and echocardiography, but she refused from genetic analyses. Two asymptomatic family members (III: 2 and III: 4) did not have any signs of HCM or DCM in echocardiography and they were not mutation carriers.

3.3. Patient with the Arg1500Trp mutation in the β-myosin heavy chain gene

The first symptoms (palpitation, dyspnea and chest pain) of the disease in the Arg1500Trp mutation carrier appeared at the age of 55 years. P-terminal force (PTF) and left ventricular hypertrophy (LVH) were detected on ECG. In echocardiography the diagnostic criteria for DCM were fulfilled, LVEDD being 70 mm and EF 32%. No ventricular hypertrophy, but secondary mitral regurgitation, was found. In coronary angiography there were no signs of coronary artery disease. After primary diagnosis medical treatment (ACE-inhibitors, β-blockers, digitalis and warfarin) was started and during 7 years of follow-up she has been stable ever since, echocardiographic parameters showing some improvement.

Her mother died at the age of 75 years due to heart failure. She had had first symptoms and signs of heart failure in her 60s. Echocardiography was not performed, but in chest X-ray cardiomegaly was detected. She had normal blood pressure and type II diabetes. There was no suspicion of coronary artery disease in her medical charts. Unfortunately, DNA sample is not available from her. The mother of the index patient had 14 siblings, but they have all died, some of them at a young age. Since DNA was not available we were not able to verify that the disease was familial in nature. The father of the index patient died in the war, and he did not have any cardiac symptoms. The daughter of the index patient is not a mutation carrier and she is also clinically healthy with normal findings in echocardiography. The clinical characteristics of the family with the Arg1500Trp mutation are presented in Table 3.

3.4. Variants in the α-tropomyosin, troponin C, I and T genes

We also screened 9 exons of α-tropomyosin, 6 exons of troponin C, 8 exons of troponin I and 16 exons of troponin T genes. Several variants in the α-tropomyosin, troponin C, I and T genes were detected. None of these variants was clearly associated with DCM, since all the variants were detected also in control patients with two exceptions (Table 1). Two variants were located in the non-coding regions of the troponin C (A→C in 3’UTR region) and troponin T (intron 6–50 bp G→T/A) genes, and therefore they are probably not disease-causing variants, because they were not located in the coding regions or splicing cites of the genes. Previously, only one variant associated with cardiomyopathy has been detected in the non-coding region of the troponin T gene (IVS 15 + 1 G→A [43]). Another variant, Lys263Arg, in exon 15 of the troponin T gene was detected, but the same variant was also found in control subjects and patients with hypertrophic cardiomyopathy excluding the possibility of disease-causing effect of the variant [43].

4. Discussion

We describe here two novel missense mutations in the β-myosin heavy chain gene, which were primarily detected in patients with a DCM phenotype. The Arg1053Gln mutation was identified later to be associated with several patients carrying a HCM phenotype. The Arg1500Trp mutation was found in a patient with classical DCM, but it was not possible to prove the familiarity of the disease. We can assume that both of these mutations can cause DCM. The disease-associating effect of the mutations is supported by the fact that neither of the mutations was detected in 150

---

Table 3

<table>
<thead>
<tr>
<th>Family</th>
<th>R1500W mutation</th>
<th>Age at the time of first symptoms</th>
<th>Age at the time of DCM diagnosis (confirmed or assumed)</th>
<th>LVEDD (mm)</th>
<th>EF (%)</th>
<th>Cardiomegaly in chest X-ray</th>
<th>LVH in ECG</th>
<th>CHF</th>
<th>In the end of follow-up (A= alive, D = dead)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I: 1</td>
<td>ND</td>
<td>60s</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
<td>D 75 years old</td>
</tr>
<tr>
<td>II: 1</td>
<td>yes</td>
<td>55</td>
<td>55</td>
<td>70</td>
<td>32</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>A 63 years old</td>
</tr>
<tr>
<td>III: 1</td>
<td>no</td>
<td>–</td>
<td>–</td>
<td>50</td>
<td>58</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>A 36 years old</td>
</tr>
</tbody>
</table>

CHF, congestive heart failure; EF, ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVH, left ventricular hypertrophy; ND, not determined; R1500Trp, substitution of arginine to tryptophan in codon 1500.
healthy controls or in the additional study group of DCM patients excluding the possibility of common polymorphism, and that both mutations affect conserved residues of the β-myosin heavy chain gene. Functional studies of the mutations are needed before clear conclusions about the disease-causing mechanisms can be established.

To our knowledge, DCM-causing mutations in the β-myosin heavy chain gene have been considered rare, and only four mutations of this kind have been found previously [3,10]. In our DCM patients the novel mutations in the β-myosin heavy chain gene seem to be rather uncommon, too. On the other hand, only one mutation in the β-myosin heavy chain gene has been previously detected among Finnish HCM patients, and this mutation explains only 3% of all HCM cases in the Eastern Finnish population [44]. In contrast, in other populations mutations in the β-myosin heavy chain gene are substantially more frequent (30%) in patients with HCM than DCM [22].

Most of the HCM-associated and all of the previously published DCM-associated β-myosin heavy chain mutations are located in the region encoding the globular head and head-rod junction of the protein [3,10,45]. The previously reported mutations (Ala223Thr, Ser532Pro, Ser642-Leu and Phe764Leu) in the β-myosin heavy chain gene causing DCM are located in the region called S1, which has binding sites for actin and ATP [3,10]. Also previously reported mutations, Arg249Gln, Lys450Glu, Leu517Met, Gln734Glu in the β-myosin heavy chain gene associated with a transition form of HCM are located in the same region [30,35]. The DCM-associated mutations in the β-myosin heavy chain gene are thought to disrupt binding between myosin and actin, decrease efficiency of contraction by altering the magnitude or polarity of transmitted movement, or alternatively decrease thermobility or affect protein folding [3,10]. The Arg1053Gln and Arg1500Trp mutations are located in different regions of the protein compared to those reported by Kamisago et al. [10], Daehmlow et al. [3], Arbustini et al. [30] and Nanni et al. [35], and probably the disease-causing mechanisms are also different in these mutations. The Arg1053Gln mutation in exon 25 is located in the S2 domain participating in the interaction between cardiac myosin-binding protein-C and β-myosin heavy chain proteins [46]. On the other hand, the Arg1500Trp mutation in exon 32 is located in the rod domain of the protein called light meromyosin (LMM), which has a role in the assembly of the thick filament [47]. In this part of the protein there are also binding sites for titin and cardiac myosin-binding protein-C [45].

In our family with the Arg1053Gln mutation, the phenotypes of the mutation carriers were variable and one family member (II: 2) probably demonstrated a transition from a HCM to a DCM-type disease. His first clinical examination was performed at the time when there was no possibility to echocardiography, and therefore, the primary diagnosis is uncertain. However, later, his phenotype and echocardiographic findings fulfilled the diagnostic criteria for DCM, although some hypertrophy of septal myocardium was found. Therefore, his disease had characteristics of a transition from a HCM to a DCM-type disease. According to previous studies patients who first have HCM-type disease and later develop DCM-type disease are often young at the onset of symptoms [25,30,32]. Our patient was only 14 years old, when cardiomyopathy was first suspected. The transition form of HCM has been shown to be associated with poor prognosis including sudden death and need for heart transplantation, and in accordance with this our patient also died of sudden cardiac death at the age of 48 years [48,49].

In the small family with the Arg1500Trp mutation, the cosegregation of the mutation with the disease could not be confirmed, and this of course is a clear limitation in our study. Our index patient had a phenotype of DCM fulfilling all the diagnostic criteria for the disease, and her mother also suffered from heart failure. Because DNA was not available from the mother the familiarity could not be verified. The only family member alive, the index patients’ daughter, is healthy, and did not carry the mutation.

In summary, we describe two novel mutations (Arg1053Gln and Arg1500Trp) in the β-myosin heavy chain gene in Finnish patients with dilated cardiomyopathy. Although mutations in the β-myosin heavy chain gene are quite uncommon in patients with DCM, they should perhaps be taken into consideration when genetic screening is performed in familial cases.

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References


