Keio Mutation Database for eye disease genes (KMeyeDB)

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ABSTRACT

A database of mutations in human eye disease genes has been constructed. This KMeyeDB employs a database software MutationView which provides graphical data presentation and analysis as a smooth user-interface. Currently, the KMeyeDB contains mutation data of 16 different genes for 18 eye diseases. The KMeyeDB is accessible through http://mutview.dmb.med.keio.ac.jp with advanced internet browsers.

INTRODUCTION

We have been involved in the identification and characterization of the genes responsible for hereditary eye diseases and have so far cloned three novel genes: myocilin (MYOC) (1), retina-specific amine oxidase (AOC2) (2,3) and immunoglobulin superfamly gene containing leucine-rich repeat (ISLR) (4) using the enriched retina cDNA library. Of these, myocilin was found to be identical to the TIGR (Trabecular meshwork-Induced Gluconeogenic Responsive) which was reported to be responsible for the chromosome 1q-linked primary open angle glaucoma (GLC1A) (5,6). Furthermore, we have found various mutations in previously established eye-disease genes in Japanese patients (7–10). To aid efficient DNA diagnosis, we have collected mutation data of the pathogenic genes for a variety of eye diseases including retinitis pigmentosa, glaucoma, corneal dystrophy, choroideremia and others (Table 1).

DATABASE AND SOFTWARE

Database was constructed for each gene as a set of hierarchical tables with formats defined in our distributed database software MutationView, which will be described elsewhere (S.Minoshima, S.Mitsuyama, S.Ohno, T.Kawamura and N.Shimizu, manuscript submitted). Currently, KMeyeDB covers 18 diseases and 16 genes as shown in Table 1. 447 mutations have been collected from 108 literature sources.

Table 2 shows all the mutation data of the MYOC gene as a typical example of KMeyeDB contents. Using MutationView software, these collected mutation data can be viewed in various ways (Figs 1, 2 and 3). Figure 1 shows a default display of gene structure window, in which each mutation is presented at the proper position of genome structure as a histogram with height proportional to case number. The type of mutation is shown as in the Symbol Table (Fig. 1, inset). It is obvious that mutations are clustered in exon 3. The additional information on each mutation such as Hereditary Pattern, Age of Onset, Ethnic Origin and Author can be obtained by the function Classify (Fig. 2). Mutations can be sorted according to Ethnic Origin (Fig. 2, right). PCR primers to amplify exons are also shown (Fig. 2, top). It is possible to change the genomic structure to cDNA or coding

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Table 2. Mutations of the MYOC gene in primary open angle glaucoma

<table>
<thead>
<tr>
<th>Mutation type</th>
<th>Mutation Position</th>
<th>Length of affected nucleotides</th>
<th>Nucleotide sequence after mutation</th>
<th>Mutation name</th>
<th>Case #</th>
<th>Symptom</th>
<th>Hereditary pattern</th>
<th>Onset age</th>
<th>Ethnic origin</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>1091</td>
<td>1</td>
<td>T</td>
<td>G364V</td>
<td>2</td>
<td>AD</td>
<td>ND</td>
<td>American</td>
<td>(6)</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>1102</td>
<td>1</td>
<td>T</td>
<td>Q368X</td>
<td>2</td>
<td>AD</td>
<td>ND</td>
<td>American</td>
<td>(6)</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>1309</td>
<td>1</td>
<td>C</td>
<td>Y437H</td>
<td>1</td>
<td>AD</td>
<td>ND</td>
<td>American</td>
<td>(6)</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>1041</td>
<td>1</td>
<td>C</td>
<td>1041T</td>
<td>4</td>
<td>AD</td>
<td>ND</td>
<td>American</td>
<td>(6)</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>1109</td>
<td>1</td>
<td>T</td>
<td>P370L</td>
<td>2</td>
<td>AD</td>
<td>10.5 (6-27)</td>
<td>French</td>
<td>(11)</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>1430</td>
<td>1</td>
<td>G</td>
<td>M77S</td>
<td>1</td>
<td>AD</td>
<td>33 (11-61)</td>
<td>French</td>
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<tr>
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<td>1</td>
<td>A</td>
<td>N480K</td>
<td>3</td>
<td>AD</td>
<td>32.3 (10-75)</td>
<td>French</td>
<td>(11)</td>
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<tr>
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<td>1498</td>
<td>1</td>
<td>T</td>
<td>HAWF</td>
<td>1</td>
<td>AD</td>
<td>31 (20-40)</td>
<td>French</td>
<td>(11)</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>736</td>
<td>1</td>
<td>A</td>
<td>G26MR</td>
<td>1</td>
<td>AD</td>
<td>20 (11-28)</td>
<td>French</td>
<td>(11)</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>1109</td>
<td>1</td>
<td>T</td>
<td>P370L</td>
<td>1</td>
<td>AD</td>
<td>21 (16-26)</td>
<td>Japanese</td>
<td>(12)</td>
<td></td>
</tr>
<tr>
<td>M</td>
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<td>A</td>
<td>G267R</td>
<td>1</td>
<td>AD</td>
<td>45</td>
<td>Japanese</td>
<td>(12)</td>
<td></td>
</tr>
</tbody>
</table>

*1 Abbreviations are as follows: M, missense; N, nonsense; P, polymorphism.
*2 Elevated intraocular pressure and optic nerve cupping in the presence of a biomicroscopically normal trabecular meshwork.
*3 Abbreviations are as follows: AD, autosomal dominant; ND, not described.
*4 The description 10.5 (6–27) means that the averaged age is 10.5 years among 6–27 years.

Figure 1. Myocilin gene mutations shown in MutationView: See text for details.
Figure 2. Classification of the myocilin gene mutation data based on ethnic origin. See text for details.

Figure 3. Myocilin gene mutation in exon 3. See text for details.

be made accessible. We are trying to expand the accessible data to other disease gene mutations in collaboration with world-wide locus-specific mutation databases (LSDBs) created by the expert curators for individual disease genes.
ACCESSIBILITY AND AVAILABILITY

Because of its high capability, access to KMeyeDB requires advanced internet browsing software including: (for Macintosh) Internet Explorer 3.0/4.0 + MRJ2.0; (for Windows95/NT) Netscape Communicator 4.03 AWT1.1, Netscape Communicator 4.05 Preview Release 1 (AWT1.1.5), Internet Explorer 3.0 SDK for Java1.5 or Internet Explorer 4.0/later; (for Solaris 2.4 or later of Sparc workstation) Netscape 4.04 JavaAWT1.1 Preview Release 2 or NetScape Communicator 4.05 Preview Release 1 (AWT1.1.5).

KMeyeDB is located at Keio University School of Medicine and is accessible via http://mutview.dmb.med.keio.ac.jp with user ID and password, which are issued after application through the same URL. The software MutationView is made available to the founders and qualified curators of LSDBs on a collaborative basis to establish a world-wide distributed database system for disease gene mutations. For inquiries, contact Shinsei Minoshima (mino@dmb.med.keio.ac.jp) or Nobuyoshi Shimizu (shimizu@dmb.med.keio.ac.jp).

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REFERENCES