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MAPPING A GENE FOR FAMILIAL HYPERTROPHIC CARDIOMYOPATHY TO CHROMOSOME 14q1

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Abstract To identify the chromosomal location of a gene responsible for familial hypertrophic cardiomyopathy, we used clinical and molecular genetic techniques to evaluate the members of a large kindred. Twenty surviving and 24 deceased family members had hypertrophic cardiomyopathy; 58 surviving members were unaffected. Genetic-linkage analyses were performed with polymorphic DNA loci dispersed throughout the entire genome, to identify a locus that was inherited with hypertrophic cardiomyopathy in family members. The significance of the linkage detected between the disease locus and polymorphic loci was assessed by calculating a lod score (the logarithm of the probability of observing coinheritance of two loci, assuming that they are genetically linked, divided by the probability of detecting coinheritance if they are unlinked). A DNA locus (D14S26), previously mapped to chromosome 14 and of unknown function, was found to be coinherited with the disease in this family. No instances of recombination were observed between the locus for familial hypertrophic cardiomyopathy and D14S26, yielding a lod score of +9.37 (θ = 0). These data indicate that in this kindred, the odds are greater than 2,000,000,001:1 that the gene responsible for familial hypertrophic cardiomyopathy is located on chromosome 14 (band q1). (N Engl J Med 1989; 321:1372-8.)

FAMILIAL hypertrophic cardiomyopathy is an idiopathic disorder of the myocardium that has an autosomal dominant pattern of inheritance.1-3 The disease is characterized clinically by myocardial hypertrophy, a wide spectrum of possible symptoms, and an annual rate of 2 to 4 percent for mortality due to sudden death,4-6 which can occur even in asymptomatic persons. Postmortem examination reveals increased myocardial mass, with myocytic and myofibrillar disarray.7,8 The diagnosis is based on typical clinical features and the demonstration of unexplained left, right, or bilateral ventricular hypertrophy on two-dimensional echocardiography.9-12 Left ventricular hypertrophy is usually asymmetric and may affect most of the ventricle or be localized. In the young, the diagnosis is often complicated because hypertrophy may not develop until after adolescent growth has been completed.13 The anatomical distribution of myocardial hypertrophy and the severity of symptoms may be quite variable, even within a family.10-13 During the past 30 years, the cardiac features of this disease have been reported widely, but the cause and molecular pathophysiology have remained speculative.

To understand the genetic basis for familial hypertrophic cardiomyopathy, we have used a molecular genetic technique to identify the chromosomal location of the disease locus in a large family. This approach has been used to identify the genetic loci responsible for more than 30 inherited disorders,14-15 including Huntington's disease, familial polyposis, cutaneous malignant melanoma–dysplastic nevus syndrome, ataxia–telangiectasia, and Duchenne's muscular dystrophy. Each disease locus has been mapped to a region of the human genome with the use of cosegregation analysis, which defines the genetic linkage between a known chromosomal location (defined by a DNA probe) and the gene responsible for the disease. Since there were neither candidate genes nor cytogenetic abnormalities to suggest the chromosomal location of the gene responsible for familial hypertrophic cardiomyopathy, we began to screen DNA probes corresponding to loci throughout the entire genome, to identify one linked to the locus for familial hypertrophic cardiomyopathy. These DNA probes recognize restriction-fragment–length polymorphisms (RFLPs) and are a subset of DNA markers used to construct a genetic-linkage map reported to span the human genome.16

A large family17 in which the gene for familial hypertrophic cardiomyopathy segregated as an autosomal dominant trait was evaluated clinically and in genetic analyses. We used 41 polymorphic DNA probes18 before identifying one (CRI-L436), derived from chromosome 14, that is linked to the locus for familial hypertrophic cardiomyopathy in this family. The chromosomal location of the disease locus suggests candidate genes that may be responsible for familial hypertrophic cardiomyopathy and provides a basis for determining whether additional genetic loci can cause this disorder independently in unrelated families.

METHODS

Cardiac Evaluation

A large French Canadian family (Fig. 1), previously evaluated by one of us,17 was selected for further evaluation. All surviving mem-
bers who were 16 years of age or older were evaluated by physical examination and 12-lead electrocardiography. Electrocardiograms were interpreted according to standard criteria. Complete two-dimensional echocardiography, with left and right ventricular views and Doppler ultrasoundography, was performed in all family members in Generation I, all children whose parents were affected, and any family member with an abnormal physical examination or electrocardiogram. Echocardiography was performed with a 2.5-MHz or 3.5-MHz transducer with an ATL mechanical sector scanner or a Hewlett-Packard phased-array system. Images were stored on VHS videotape for subsequent analysis. Measurements of wall thickness and cavity dimensions and the presence or absence of systolic anterior motion of the mitral valve were determined according to established protocols. The diagnosis of hypertrophic cardiomyopathy was based on the two-dimensional echocardiographic demonstration of unexplained left, right, or bilateral ventricular hypertrophy and was made without knowledge of DNA patterns. None of the family members evaluated had a history of systemic hypertension or a resting blood pressure greater than 140/90 mm Hg.

Genetic Mapping Studies

Lymphoblastoid cell lines were established by Epstein-Barr virus transformation of blood samples obtained from each family member indicated in Figure 1. The cell lines were expanded, and the DNA was prepared for use in Southern blot analyses as described previously. In brief, the samples of DNA were digested with a restriction enzyme, fractionated on 1 percent agarose gels, and transferred to GeneScreen filters (Dupont) for hybridization. A panel of approximately 120 DNA probes that identify RFLPs was made available to us for these studies by Collaborative Research. Each DNA probe recognizes a particular locus; CRI-L436, CRI-L329, and CRI-C70 recognize loci D14S26, D14S25, and D14S24, respectively. These probes and others, specifically indicated, were used in linkage analyses. DNA probes were labeled by the hexamer priming procedure to a specific activity of more than 10^6 cpm per microgram and hybridized to GeneScreen filters as described elsewhere. Filters were washed under conditions of high stringency (low salt, high temperature: 15 mM sodium chloride, 1.5 mM sodium citrate, and 0.1 percent sodium dodecyl sulfate, at 65°C) and subjected to autoradiography for 24 to 72 hours with intensifying screens (Dupont Lightning Plus) at -70°C.

To determine whether the DNA probes cosegregated with the locus for familial hypertrophic cardiomyopathy, we used the LINKAGE computer program. Two of us analyzed the restriction-fragment pattern identified by a DNA probe, independently and without knowledge of each family member's disease status, to determine the genomic alleles present in each family member. There was complete agreement in the assignment of alleles between reviewers. A set of lod (logarithm of the odds) scores was then ascertained for each DNA probe at given recombination fractions. The lod score indicates the statistical likelihood that two loci are linked. A lod score is calculated from the ratio of the probability of inheriting two gene loci (i.e., that responsible for familial hypertrophic cardiomyopathy and a particular allele), given a distance of $\theta$ between these loci, to the probability of inheriting both loci if they are not linked in the genome ($\theta = 0.5$). Lod scores vary as a function of $\theta$, which is the frequency with which two loci recombine during meiosis and can be converted to a genetic distance (defined in centimorgans, Cm) within the genome. Two loci are 1 Cm apart (approximately 10^6 base pairs of DNA) if they recombine in 1 percent of all meioses. A lod score above +3 indicates that the observed data are 1000-fold more likely to occur, assuming two loci are linked at a given distance. A lod score of less than −2 is generally accepted as evidence of nonlinkage between a pair of loci at a given distance.

Multipoint analyses were performed with use of the LINKAGE program, assuming that the penetrance of the gene for familial hypertrophic cardiomyopathy was 0.95 in each family member over the age of 16. Allele frequencies were determined independently in the population studied and used in linkage calculations.

Results

Clinical Analyses

To identify a DNA marker linked to the gene responsible for familial hypertrophic cardiomyopathy, 78 members of a large Canadian family were evaluated clinically. Sixty-four were siblings, parents, or offspring of an affected person (Fig. 1). Fourteen were the children of unaffected parents and are not shown in Figure 1. On the basis of a previous clinical evaluation, postmortem examination, or both, 24 deceased members of the family had hypertrophic cardiomyopathy. Twenty of these died prematurely (before 45 years of age). Death was sudden in seven, disease related in five, and noncardiac in two; in six, the mode of death was not ascertained.

Hypertrophic cardiomyopathy was diagnosed in 20 living family members. The clinical features of these members are shown in Table 1. Four affected
family members were asymptomatic, whereas three had undergone septal myectomy for refractory symptoms. All but three affected family members fulfilled the echocardiographic criteria for left ventricular hypertrophy (80 percent), with an increase in the maximal thickness of the left ventricular wall (mean, 20 mm); right ventricular hypertrophy (40 percent); and enlargement of the left atrium (mean, 44 mm). Two family members were classified as affected despite the absence of echocardiographic evidence of left ventricular hypertrophy. Subject II-4 had undergone septal myectomy 17 years earlier, with documented regression of left ventricular hypertrophy in association with severe aortic regurgitation and progressive impairment of left ventricular systolic function. Subject III-6 had right ventricular hypertrophy (right-ventricular-wall thickness, 12 mm), with hyperdynamic left ventricular systolic function and incomplete systolic anterior motion of the mitral valve. Five of the 20 affected family members had evidence of a resting left ventricular gradient between 20 and 100 mm Hg on Doppler ultrasonography, echocardiography, or previous invasive hemodynamic examination.

Fifty-eight family members had no clinical, electrocardiographic, or two-dimensional-echocardiographic features of hypertrophic cardiomyopathy. Of these, one was found to have a dilated cardiomyopathy of the right ventricle, and another had a congenital ventricular septal defect.

**Gene-Mapping Studies**

Because several reports suggested that the locus for familial hypertrophic cardiomyopathy was linked to the major histocompatibility complex, we began our analysis with probes that recognize polymorphisms on chromosome 6q. None of the DNA probes analyzed—pHLA-1, pXIIIa, CR1-L171, or CR1-R125, which detect loci near the major histocompatibility complex—showed evidence of close linkage to the locus for familial hypertrophic cardiomyopathy (lod score <2.0 at θ = 0.5; Table 2).

For the systematic screening of the entire human genome for the location of the locus responsible for familial hypertrophic cardiomyopathy, we used a subgroup of DNA markers that link more than 95 percent of the human genome. This subgroup was selected on the basis of their heterozygosity, or ability to detect RFLPs and spacing along the various chromosomes. The chromosomal location of these DNA probes was established by cytogenetic in situ hybridization, somatic cell–hybrid mapping panels, or determination of linkage to previously assigned loci.

DNA derived from lymphoblastoid cell lines was digested with restriction enzymes known to reveal polymorphisms and transferred to GeneScreen filters for hybridization to probes. From the panel of DNA probes, we screened 41 (Table 2 and unpublished data). Of these, 33 probes yielded data that were not consistent with linkage to the locus for familial hypertrophic cardiomyopathy with a distance of 5 cm (lod score <2). Seven probes did not yield sufficient information to determine their relation to the locus for familial hypertrophic cardiomyopathy.

The locus D14S26 was co-inherited with the locus for familial hypertrophic cardiomyopathy by each member of the Canadian kindred (Table 2). DNA probe CRI-L436 recognizes a *TaqI* endonuclease polymorphism at locus D14S26 and identifies two alleles (a 4.2-kb fragment [allele 1] or a 2.2-kb and a 1.8-kb fragment [allele 2]) as well as a number of constant fragments. The alleles defined by CRI-L436 for each family member are indicated in Figure 1. The lod scores for the linkage of CRI-L436 to the locus for familial hypertrophic cardiomyopathy, assuming various recombination distances between the disease locus and the CRI-L436 locus, are given in Table 2. We observed no recombination between the locus for fa-

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**Table 1. Clinical Characteristics of Affected Family Members.**

<table>
<thead>
<tr>
<th>SUBJECT No.</th>
<th>AGED SEX</th>
<th>CHEST PAIN</th>
<th>DYSPNEA*</th>
<th>SYNCOPE</th>
<th>ELECTROCARDIOGRAM†</th>
<th>2-D ECHOCARDIOGRAM†</th>
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<td></td>
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<td></td>
<td></td>
<td>SAM</td>
<td>SIZE</td>
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<td>I-1</td>
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<td>+</td>
<td>III</td>
<td>+</td>
<td>R</td>
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<td>I-2</td>
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<td>II</td>
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<td>–</td>
<td>–</td>
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<tr>
<td>I-7</td>
<td>45/F</td>
<td>+</td>
<td>III</td>
<td>–</td>
<td>–</td>
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<tr>
<td>I-12</td>
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<td>+</td>
<td>III</td>
<td>–</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>I-16</td>
<td>44/F</td>
<td>–</td>
<td>II</td>
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<td>II</td>
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<td>–</td>
<td>30</td>
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<td>I-5</td>
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<tr>
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<td>+</td>
<td>II</td>
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<td>–</td>
<td>12</td>
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<tr>
<td>I-7</td>
<td>22/F</td>
<td>+</td>
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<td>–</td>
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<td>I-16</td>
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<td>II</td>
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<tr>
<td>I-20</td>
<td>22/M</td>
<td>+</td>
<td>IV</td>
<td>–</td>
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<td>I-21</td>
<td>23/M</td>
<td>+</td>
<td>I</td>
<td></td>
<td>–</td>
<td>30</td>
</tr>
<tr>
<td>I-22</td>
<td>22/F</td>
<td>–</td>
<td>I</td>
<td></td>
<td>–</td>
<td>34</td>
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</tbody>
</table>

*The degree of dysepsa present was based on the New York Heart Association functional classification.
†BBB denotes bundle-branch block, ABN Q abnormal Q wave, LVH ≥STÅ left ventricular hypertrophy with voltage criteria and/or repolarization changes, R, right; and L, left.
‡2-D denotes two-dimensional, max LVWT maximal thickness of the left ventricular wall, RVH right ventricular hypertrophy, SAM systolic anterior motion of the mitral valve, LA left atrial, ++ complete, and + incomplete.
Table 2. Comparison of Lod Scores for Familial Hypertrophic Cardiomyopathy Analyzed with DNA Probes from Chromosomes 6 and 14.

<table>
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<th>0.20</th>
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<td></td>
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<td></td>
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<tr>
<td>Factor XIIIa</td>
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<td>-2.436</td>
<td>-1.491</td>
<td>-0.648</td>
<td>-0.266</td>
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<tr>
<td>HLA-A</td>
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<td>-4.770</td>
<td>-2.850</td>
<td>-1.170</td>
<td>-0.423</td>
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<tr>
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<td>-4.800</td>
<td>-2.582</td>
<td>-0.710</td>
<td>-0.022</td>
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<tr>
<td>L322</td>
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<td>-4.020</td>
<td>-2.362</td>
<td>-0.901</td>
<td>-0.252</td>
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<tr>
<td>Chromosome 14</td>
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<td></td>
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<tr>
<td>L1113</td>
<td>-∞</td>
<td>-4.517</td>
<td>-2.666</td>
<td>-1.082</td>
<td>-0.387</td>
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<tr>
<td>L1013</td>
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<td>-1.059</td>
<td>-0.300</td>
<td>-0.177</td>
<td>+0.206</td>
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<tr>
<td>C70</td>
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<td>-0.382</td>
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<tr>
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<td>+8.066</td>
<td>+7.158</td>
<td>+6.210</td>
<td>+4.183</td>
<td>+2.041</td>
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</table>

*θ* denotes the frequency of recombination.

Familial hypertrophic cardiomyopathy in this pedigree and this probe. The maximal lod score (+8.07) was calculated at a recombination distance between the disease locus and CRI-L436 of 0 cM.

Having found this linkage, we analyzed two other anonymous probes, CRI-L329 and CRI-C70, located 4 cM and 25 cM from CRI-L436, respectively. Although probe CRI-C70 provided no information about the linkage of the CRI-C70 locus to the locus for familial hypertrophic cardiomyopathy (maximum lod score, +0.1 at θ = 0.32), probe CRI-L329 provided weak evidence in favor of linkage (Table 2). A single recombinant event was detected between probe CRI-L329 and the locus for familial hypertrophic cardiomyopathy, with a maximal lod score of +1.1 at θ = 0.1 cM. Although probes CRI-L436 and CRI-L329 define closely linked loci, the polymorphisms detected by probe CRI-L329 were relatively uninformative in this kindred and thus provided only weak evidence in favor of linkage to the locus for familial hypertrophic cardiomyopathy.

We determined the linkage relation between the three loci recognized by these DNA probes and the disease locus in this family by multipoint linkage analysis, using the LINKAGE computer program. This program analyzes the cosegregation of several markers simultaneously with the disease locus. Figure 2 shows the results of the multipoint linkage analyses. The curve represents the lod score achieved if the locus for familial hypertrophic cardiomyopathy resides at any given position along this region of chromosome 14. These data predict that the disease locus is 10-fold more likely to be located distal to CRI-L329 than between CRI-L329 and CRI-C70. With the use of multipoint analysis, a maximal lod score of +9.37 was achieved at the CRI-L436 locus (θ = 0), suggesting that in this family, the probability of the linkage of the locus for familial hypertrophic cardiomyopathy to this region is greater than 10⁹.¹

The assignment of CRI-L436 to chromosome 14 is based on analyses of panels of rodent–human hybrid cells containing various human chromosomes. Probes CRI-L329 and CRI-C70 were assigned to chromosome 14 on the basis of linkage to CRI-L436.²¹ These three probes define loci that are not linked to markers located at 14q32.¹⁶ We also found that the gene responsible for familial hypertrophic cardiomyopathy is not closely linked to CRI-L1113 and CRI-L1013, which map near 14q32 (Table 2; multipoint linkage analysis not shown). The gene encoding the α chain of the T-cell receptor has been cytogenetically mapped to 14q11²⁹ and is approximately 20 cM from D14S26 (identified by probe CRI-L436). Given this close linkage, we conclude that the gene responsible for familial hypertrophic cardiomyopathy in this kindred is located on chromosome 14 band q1. Figure 3 shows the relative location of the disease locus on chromosome 14, and the loci identified by related probes.

**Discussion**

We have demonstrated that locus D14S26 is genetically linked to the locus responsible for familial hypertrophic cardiomyopathy in a large family with this disease. D14S26 has been previously mapped to chro-
familial hypertrophic cardiomyopathy. A beta-spectrin gene has been mapped to chromosome 14, and defects in this gene can cause spherocytosis. On the basis of the linkage data presented here, we hypothesize that this family may have an abnormality of chromosome 14, producing both phenotypes, and suggest that in two unrelated families, the locus for familial hypertrophic cardiomyopathy is on chromosome 14.

To ascertain whether mutations in the same genetic locus are responsible for familial hypertrophic cardiomyopathy in other families, further linkage analyses are required. To date, we have studied three other unrelated families in which affected members have clinical features similar to those of affected members in the Canadian kindred. Data on the genetic relation between the disease locus in these three families and the DNA locus defined by probe CRI-L436 support the linkage model (combined lod score, +1.8). No recombination was observed between the familial locus in these families and this probe. There is a 1:63 probability of obtaining the observed pattern of inheritance of the gene responsible for the disease and the locus identified by CRI-L436 if these are not linked. Although further analyses are required with additional probes and families, these data suggest that mutations in a single genetic locus present on chromosome 14 are responsible for familial hypertrophic cardiomyopathy in four unrelated families.

The identification of a DNA marker that is linked to the locus responsible for familial hypertrophic cardiomyopathy in several families will be of great value clinically. At present, prenatal diagnosis of familial hypertrophic cardiomyopathy is not possible, and accurate diagnosis in young children with an affected parent can be difficult. DNA analyses with probes such as CRI-L436 and others more closely linked to the locus for familial hypertrophic cardiomyopathy will eventually allow affected children to be distinguished from unaffected children. Early diagnosis of the disorder may then improve strategies for therapy and prognosis. In addition, analyses with closely linked probes may elucidate the relation between familial and apparently sporadic cases of hypertrophic cardiomyopathy.

The definition of a DNA marker that is linked physically to a locus for familial hypertrophic cardiomyopathy provides a valuable reagent for studies aimed at identifying the gene that causes this disease. Research by others has suggested that abnormal adrenergic function may be important in causing hypertrophic cardiomyopathy, and recent work has documented an increase in the number of calcium-antagonist receptors in atrial tissues of patients with this disease. Since the chromosomal location of the gene encoding these receptors is unknown, it is not feasible to test this hypothesis. Both neurofibromatosis and aniridia with catalase deficiency are associated with a cardio-

![Figure 3. Conventional Banding Pattern of Human Chromosome 14 on Giemsa Staining.](image)

The positive bands are black, the centromeric region is broadly hatched, and the nucleoli-organizer region is finely hatched. The discontinuity in the short arm reflects polymorphism in the size of this region. The cytogenetically defined location of the gene encoding the a chain of the T-cell receptor (TCRA) at band q11.30,31 and the location of the q1 band are indicated by the double-headed arrow. A genetic map of probes that identify loci in the q1 region is shown. The distances between these loci are given in centimorgans. An unrelated region of chromosome 14 identified by probes CRI-L1113 and CRI-L1013 is shown. Linkage data suggest that the gene for familial hypertrophic cardiomyopathy (FHC) is located in band q1, close to the locus defined by CRI-L436.

Chromosome 14 is closely linked to a locus (the a chain of the T-cell receptor) in band q11, thereby assigning the locus for familial hypertrophic cardiomyopathy in this kindred to this region of the genome (Fig. 3).

There is considerable heterogeneity in symptoms, prognosis, and the severity and distribution of myocardial hypertrophy in affected persons from related and unrelated families. Whether these clinical observations are due to differences in the expression of a single gene responsible for hypertrophic cardiomyopathy in all families or to several genes that yield similar phenotypes can now be tested. Recently, a family was described with both hereditary spherocytosis and
myopathy that is clinically similar to familial hypertrophic cardiomyopathy. Because the genes responsible for these disorders map to chromosome 17 and 11, respectively, our data suggest that these clinically coincident events are not explained by genetic linkage of responsible loci.

A number of genes that are thought to play a part in cardiac hypertrophy have been mapped to chromosome 14. Genes for the heavy chains (α and β) of cardiac myosin have been mapped to 14q11.2–q13.1,11,12 Our linkage analyses and these genomic location are particularly provocative since myosin heavy-chain gene expression is altered in rodents with cardiac hypertrophy.13 Future studies should demonstrate whether the myosin heavy-chain gene is closely linked to the locus for familial hypertrophic cardiomyopathy. Two other candidate genes — the gene for heat-shock protein (HSP70) and the protooncogene c-fos — map to chromosome 14. The linkage of c-fos, which maps to 14q24–31,14 to the locus for familial hypertrophic cardiomyopathy is unlikely, given our data showing nonlinkage to probes derived from 14q32. In the development of myocardial hypertrophy, the induction of heat-shock proteins occurs early and may be important etiologically.15 The gene encoding heat-shock protein has been mapped to 14q22–24;16 in our preliminary analyses, no linkage to the locus for familial hypertrophic cardiomyopathy was detected. As other candidate genes are mapped to chromosome 14, one responsible for the disease may be identified. The eventual isolation and characterization of the gene responsible for familial hypertrophic cardiomyopathy should provide new insights into the molecular and biochemical processes that determine the growth of myocardial cells.

We are indebted to Ms. Rosa Maria Diaz-Ferland, Dr. Richard Germain, Collaborative Research, and family members, without whose invaluable assistance these studies would have been impossible; to Drs. T. Glaser, D. Housman, P. Green, and C. Helms for insightful discussions and encouragement; to Ms. S. Selvaraj for her expert assistance in cell-culture work; and to Dr. U. Grundmann and Behringwerke (Marburg) for providing the factor XIIa probe.

References

SPECIAL ARTICLE

THE EFFECT OF THE MEDICARE PROSPECTIVE PAYMENT SYSTEM ON THE ADOPTION OF NEW TECHNOLOGY

The Case of Cochlear Implants

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Abstract Since the advent of Medicare’s prospective payment system, beneficial but cost-increasing medical advances have been systematically assigned to existing diagnosis-related groups (DRGs) that do not cover the costs of the new technology. Recent evidence suggests that such underpayment reduces the rate at which hospitals adopt that technology. Safeguards designed to offset the negative incentives of underpayment, including the recalibration of DRG values, update factors, and the allowance of Medicare profits, appear not to have worked.

We studied the case of cochlear implantation. Years after Food and Drug Administration approval and a favorable decision about Medicare coverage, payment for the device remains well below its average cost, and many hospitals ration the availability of the device to Medicare patients because of the financial losses involved. Eventually, so few patients received the implant that the original manufacturer discontinued its production.

Under the DRG system, negative payment incentives compete with clinical considerations when hospitals and physicians decide whether to adopt specific cost-increasing new forms of technology of proved value. Other payment mechanisms that do not insert arbitrary financial considerations into specific treatment decisions should be considered instead. (N Engl J Med 1989; 321: 1378-83.)

HEARING loss is the most prevalent chronic physical disability in the United States.1 It is particularly common among elderly people; according to estimates, 30 percent of those over 65 years of age and 50 percent of those over 85 have important hearing handicaps.2,3 In this population, 68,000 people are thought to be postlingually deaf (that is, their deafness occurred after the development of speech) and profoundly deaf, with bilateral speech thresholds over 97 decibels.4 Hearing disabilities can exacerbate the social isolation of many older citizens, contributing to depression and disorientation.

Cochlear implantation does not restore hearing to normal levels, but it permits meaningful improvement in useful hearing, particularly for safety and warning sounds, as well as for the human voice.5,6 After extensive preoperative evaluation, one or more electrodes are implanted in the cochlea by specially trained otolaryngologists. The portion of the device that processes speech is fitted on an outpatient basis weeks after surgery; a lengthy rehabilitation follows.7 Neither the techniques used in the selection and rehabilitation of the patients nor the design of the device has reached technological maturity.

DETERMINATION OF MEDICARE COVERAGE

On November 26, 1984, the Food and Drug Administration approved the design of a single-channel device for cochlear implantation for general distribution to postlingually deaf adults. The event was reported on the front page of the New York Times and in the Wall Street Journal, the Washington Post, and other newspapers nationwide. President Reagan sent congratulatory letters to 3M, the manufacturer of the device, and to Dr. William House, its chief inventor. From the