The localization of $G6pd$, glucose-6-phosphate dehydrogenase, and $mdx$, muscular dystrophy in the mouse X chromosome

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Summary

A low activity mutant of glucose-6-phosphate dehydrogenase, $G6pd^{m/Neu}$ has been used to position $G6pd$ in the mouse X chromosome. Linkage tests with tabby, Ta and harlequin, Hq, indicate a likely gene order of $Hq$-$G6pd$-$Ta$. Muscular dystrophy, $mdx$, has been located by two- and three-point crosses using $Hprt$, $Pgk-1$ and $Mo^{10}$ and suggest a gene order of $Hprt$-$mdx$-$Pgk-1$-$Mo^{10}$. Together with existing linkage data a tentative order for the seven loci is $Hq$-$Hprt$-$G6pd$-$mdx$-$Ta$-$Pgk-1$-$Mo^{10}$. The relative positions of $G6pd$ and $mdx$ have not been directly tested and $G6pd$ is assigned provisionally proximal to $mdx$. In the three point test using $Hq$, $G6pd$ and $Ta$ the recombination frequency found between $Hq$ and $Ta$ was 9.9 ± 2.6%, substantially less than the value of 20.5 ± 2.1% reported by Isaacson et al. (1974).

1. INTRODUCTION

Evidence for the X-chromosome assignment of glucose-6-phosphate dehydrogenase, $G6pd$, in the mouse has come from gene dosage (Epstein, 1969; Chapman & Shows, 1976) and somatic cell studies. Up until recently its position in the linkage map could not be established by linkage studies because no genetic variants were available but Martin-DeLeon et al. (1984) have located $G6pd$ to the A region of the cytogenetic map by in situ hybridization. This result was supported by recombination data from two-point crosses (Peters & Ball, 1985) using a $G6pd$ mutant with lowered activity, induced by ethylnitrosourea (Pretsch et al. 1988). The proximal position of $G6pd$ was confirmed by pedigree and recombinational analysis using a molecular marker for $G6pd$ (Avner et al. 1987; Brockdorff et al. 1987a,b; Chamberlain et al. 1987). In this paper we present further linkage data from two-point crosses and describe the results from three-point crosses.

Muscular dystrophy, $mdx$, is an X-chromosome-linked myopathy in the mouse identified in a C57BL/10 substrain (Bulfield et al. 1984). We present evidence that $mdx$ is closely linked to $G6pd$ on the X chromosome. From the map position, as well as histological characteristics, it may be deduced that $mdx$ may either be homologous to DMD, muscular dystrophy Duchenne type, or to the late onset Emery–Dreifuss muscular dystrophy in humans. The recent finding that dystrophin is absent in DMD-affected individuals and in $mdx$ mice supports homology of DMD and $mdx$ (Hoffman et al. 1987a,b).

2. Materials and methods

The original animal with a mutant form of glucose-6-phosphate dehydrogenase (EC 1.1.1.49) was a female derived from a mutagenesis experiment carried out in Neuherberg (Pretsch et al. 1988). In the experiment (102/E1×C3H/E1)F₁ male mice were injected with 250 mg/kg ethylnitrosourea, mated to tester stock females and the activity levels of ten enzymes were measured in the offspring. The breeding regime was such that any induced mutations would have arisen in spermatogonial stem cells. The glucose-6-phosphate dehydrogenase activity in the blood of the original mutant was 60% of normal and subsequent breeding tests showed that the mutant was heterozygous for an allele determining normal activity ($G6pd^+$) and an allele determining low activity ($G6pd^−$).
(G6pd<sup>-/-<sub>Neu</sub></sup>), and that these alleles were at an X-linked locus (Pretsch et al. 1988). Homozygous and hemizygous descendants of the original mutant were sent to the MRC Radiobiology Unit for linkage testing with other X chromosome markers.

For the initial linkage tests females homozygous for the mutant allele, G6pd<sup>-/-<sub>Neu</sub></sup>, were crossed to males carrying either tabby, Ta, or harlequin, Hq two loci in the proximal half of the X-chromosome (Lyon, 1987a). Hybrid female progeny were crossed to (C3H/HeH×101/H)<sub>F1</sub> males and both male and female offspring classified for either Ta and G6pd or Hq and G6pd. For a subsequent three-point test, two female recombinants +G6pd<sup>-/-<sub>Neu</sub></sup>Ta/+G6pd<sup>+</sup> were crossed to HqG6pd<sup>+</sup>/Y males. Then the +G6pd<sup>-/-<sub>Neu</sub></sup>Ta/HqG6pd<sup>+</sup> female offspring were crossed to +G6pd<sup>+</sup>/+Y males of either the inbred strains C3H/HeH or 101/H or the hybrid (C3H/HeH×101/H)<sub>F1</sub>. Male offspring of this cross were scored for Hq, G6pd and Ta. G6PD was assayed and haemoglobin concentration measured using an automatic enzyme analyser (ACP 5040, Eppendorf, Hamburg, FRG) as described by Charles & Pretsch (1986).

For linkage tests of X-linked muscular dystrophy, mdx, with the visible marker genes harlequin, Hq, and blotchy, Mo<sup>bl°</sup>, males carrying mdx were crossed to females carrying Hq or Mo<sup>bl°</sup>. Hybrid female progeny were backcrossed to males carrying mdx. Then the hybrid female progeny Hprt<sup>a</sup>+Pgk-<sup>1a</sup>; homozygous for Hprt<sup>a</sup> and Pgk-<sup>1a</sup>. Hemizygous and mutant homozygotes have very low G6PD activities; 12 and 9% of normal respectively (Table 1). The mean activity in heterozygotes was intermediate; 56% of normal (Table 1). These results show reasonable agreement with those of Pretsch et al. (1984a, b) and Pretsch et al. (1988) who reported that hemizygous, heterozygous and homozygous mutants had 20, 60 and 15% normal G6PD activity in blood respectively. Charles & Pretsch (1984a, b) and Pretsch et al. (1988) also reported that haematological parameters did not show significant differences between mutant and wild type and this was confirmed in the present study.

In backcross males from the linkage tests the activity levels formed a non-overlapping bimodal distribution with peak means of a similar order to those found in parental stocks (Table 1, Fig. 1a). The low activity mutant of glucose-6-phosphate dehydrogenase thus segregates as an allele of a single X-linked gene as demonstrated by Pretsch et al. (1988). Among backcross males a greater number were found

### Table 1. Glucose-6-phosphate dehydrogenase activity levels in blood

| Source of blood | Division of progeny | n | Specific activity<sup>a</sup> (mean ± s.E.) |
|-----------------|---------------------|---|--------------------------------------------|
| G6pd<sup>+</sup>/Y | 11 | 2-58 ± 0-12 |
| G6pd<sup>-/-</sub>Neu<sup>/</sup> | 12 | 21-36 ± 0-60 |
| G6pd<sup>-/-<sub>Neu</sub>/G6pd<sup>-/-</sub>Neu<sup></sup></sup> | 11 | 22-49 ± 0-50 |
| G6pd<sup>-/-<sub>Neu</sub>/G6pd<sup>+</sup></sup> | 13 | 12-56 ± 0-73 |
| Backcross | | | |
| G6pd<sup>-/-<sub>Neu</sub>/G6pd<sup>+</sup> X G6pd<sup>+</sup>/Y | | | |
| Males | Low | 139 | 3-71 ± 0-11 |
| | High | 189 | 24-18 ± 0-25 |
| Females | Intermediate | 55 | 11-93 ± 0-30 |
| | High | 51 | 21-20 ± 0-28 |

<sup>a</sup>Enzyme activity measured as μmol/min/g haemoglobin.
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Table 2. Recombination between Hq and G6pd

| Offspring (parental mating + G6pd<sup>m</sup>/Y/Hq G6pd<sup>x</sup> + G6pd<sup>y</sup>/Y) | Non-recombinant | Recombinant |
|-------------------------------------------------|-----------------|-------------|
| Experiment 1                                      |                 |             |
| + G6pd<sup>m</sup>/Y/Y                           | 197             | 1           |
| Hq G6pd<sup>y</sup>/Y/Y                          | 28              | 1           |
| + G6pd<sup>m</sup>/m<sup>1</sup>Neu/+ G6pd<sup>y</sup> | 17              | 2           |
| Hq G6pd<sup>y</sup>/ + G6pd<sup>y</sup>/Y         | 17              | 0           |
| Total                                           | 83              | 4           |
| Experiment 2                                      |                 |             |
| Hq G6pd<sup>y</sup>/Y/Y                          | 70              | 2           |
| + G6pd<sup>m</sup>/m<sup>1</sup>Neu/Y            | 7               | 0           |

From Exp 1, recombination frequency ± S.E. = 4/87 = 4.6 ± 2.3%.
From Exp 2, recombination frequency ± S.E. = 2/79 = 2.5 ± 1.8%.
From Expts 1 and 2 combined, recombination frequency ± S.E. = 6/166 = 3.6 ± 1.5%.

(ii) Linkage of G6pd

In Expt 1 of the two-point linkage test with Hq, (Table 2) both male and female offspring were tested for G6PD. Not all females could be classified with certainty, for the G6PD activities in 4 of 40 female offspring tested fell in the region of overlap of activities found in normal homozygotes and heterozygotes and the results from those four females were discarded. All males could be classified with certainty and therefore in Expt 2 only male offspring were tested (Table 2). In addition, in Expt 2, Hq/Y males were chosen preferentially for enzyme assay because an additional aim of this experiment was to find a recombinant Hq G6pd<sup>m</sup>/m<sup>1</sup>Neu/Y male that could be used in a three-point cross with Ta.

In Expt 1, 87 mice were scored for Hq and G6pd and four recombinants were found, giving a recombination frequency of 4.6 ± 2.3%. In Expt 2, two recombinants were found among 79 offspring giving a recombination frequency of 2.5 ± 1.8%. Since there is reasonable agreement between results of the two experiments, the data from Expts 1 and 2 were combined and gave a recombination frequency between Hq and G6pd of 3.6 ± 1.5% with a 95% confidence interval of 0.7–6.5%.

In the two-point linkage test with Ta (Table 3) 181 offspring, of which 86 were females, were analysed for G6PD activity levels. Seventeen females could not be classified with certainty for G6PD because the enzyme activity levels fell in the region of overlap for activities

with high G6PD activity levels (G6PD-A) than with low, because, in one experiment involving Hq, males carrying the marker were selected for assay rather than wild type males and in the absence of recombination Hq/Y mice were expected to have high G6PD activity (Table 2). When the data from these mice were excluded there is no excess of males which are G6PD-A. In backcross females the activity levels,
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Table 3. Recombination between G6pd and Ta

| Offspring (parental mating G6pd\textsuperscript{a\textit{m}1\textit{Neu}} + /G6pd\textsuperscript{Ta} \times G6pd\textsuperscript{a} + /Y) | Non-recombinant | Recombinant |
|-------------------------------------------------|----------------|-------------|
| G6pd\textsuperscript{a\textit{m}1\textit{Neu}} + /Y | 54 | 2 |
| G6pd\textsuperscript{Ta}/Y | 37 | 2 |
| G6pd\textsuperscript{a\textit{m}1\textit{Neu}} + /G6pd\textsuperscript{a} + | 36 | 2 |
| G6pd\textsuperscript{Ta}/G6pd\textsuperscript{a} + | 28 | 4 |
| Total | 155 | 10 |

Recombination frequency ± s.e. = 10/165 = 6.1 ± 1.9%.

Table 4. Recombination between Hq, G6pd and Ta

| Male offspring (parental mating + G6pd\textsuperscript{a\textit{m}1\textit{Neu}} Ta/Hq G6pd\textsuperscript{a} + \times + G6pd\textsuperscript{a} + /Y) | n |
|-------------------------------------------------|---|
| Non-recombinant | 59 |
| Hq\textsuperscript{a} G6pd\textsuperscript{a} + /Y | 59 |
| Single recombinant 1, Hq–G6pd | 6 |
| + G6pd\textsuperscript{a} + /Y | 3 |
| Single recombinant 2, G6pd–Ta | 2 |
| + G6pd\textsuperscript{a\textit{m}1\textit{Neu}} + /Y | 2 |
| Total | 131 |

Recombination R.F ± s.e. (%) Confidence interval (95%)

| Hq–G6pd | 9/131 | 69 ± 2.2 | 2.9 – 8.2 |
| G6pd–Ta | 4/131 | 3.1 ± 1.5 | 2.6 – 7.8 |
| Hq–Ta | 13/131 | 9.9 ± 2.6 | 5.4 – 16.4 |

Table 5. Recombination between Hq and mdx

| Offspring (parental mating Hq + / + mdx/ x + + mdx/ Y) | Non-recombinant | Recombinant |
|-------------------------------------------------|----------------|-------------|
| Hq+/Y | 30 | 6 |
| +mdx/Y | 58 | 9 |
| Hq+/+mdx | 35 | 9 |
| +mdx+/+mdx | 49 | 9 |
| Total | 172 | 33 |

Recombination frequency ± s.e. = 33/205 = 16.1 ± 2.6%; 95% confidence interval, 11.3–21.9%.

(iii) Linkage of mdx

Earlier experiments had located X-linked muscular dystrophy, mdx, to the Hq–Bpa region of the mouse X-chromosome (Bulfield et al. 1984). Further two-point and three-point crosses were carried out here in order to position mdx more precisely. In the linkage test with Hq (Table 5) there was a deficiency of hemizygotes carrying Hq(36 Hq: 67+: x/\chi^2 = 8.74, \ p = 0.0031) and an excess of males carrying mdx (64 mdx: 39+: x\chi^2 = 5.59, \ p = 0.018). The reasons for these deviations from expected 1:1 segregations are not clear. Overall, considering both male and female offspring, 33 recombinants were found among 205 mice scored giving a recombination frequency of 16.1±2.6%, with a 95% confidence interval of 11.3–21.9%. Among female offspring the segregation at both Hq and mdx does not deviate from 1:1, and the estimate of recombination was 18/102 =
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Table 6. Recombination between mdx and Mo^{b10}

| Offspring (parental mating mdx + / + Mo^{b10} × mdx + /Y) | Non-recombinant | Recombinant |
|----------------------------------------------------------|-----------------|-------------|
| mdx + /Y                                                  | 65              | 3           |
| + Mo^{b10}/Y                                              | 43              | 5           |
| mdx + /mdx +                                             | 59              | 3           |
| + Mo^{b10}/mdx +                                         | 43              | 11          |
| Total                                                    | 210             | 22          |

Recombination frequency ± S.E. = 22/232 = 9.5 ± 1.9%; 95% confidence interval, 60–140%.

17.6 ± 3.8%, with a 95% confidence interval of 10.8–26.4%.

In the two-point cross with Mo^{b10} (Table 6), there was a deficiency of both male and female offspring carrying Mo^{b10} (92 Mo^{b10}; 140+: x^2 = 9.52; p = 0.0020). Overall 22 recombinants were found among 232 offspring giving a recombination frequency of 9.5 ± 1.9%, with a 95% confidence interval of 60–140%. If the recombination frequency is estimated using offspring which do not carry Mo^{b10}, the recombination frequency is slightly higher (17.6 ± 3.8%, with a 95% confidence interval of 10.8–26.4%).

For the three-point test the mdx phenotype was identified by elevated levels of muscle creatine kinase (CK) activity in circulating blood and the distribution of blood plasma CK activities in backcross progeny is shown in Fig. 2. The levels of CK activity form a bimodal distribution with +/mdx and +/Y progeny less than 90 units of activity, and mdx/mdx or mdx/Y progeny greater than 90 units.

Table 7. Recombination between Hprt, mdx and Pgk-1

| Offspring (parental mating Hprt^+ + Pgk-1^*/Hprt^+ mdx Pgk-1^*/Hprt^+ mdx Pgk-1^*/Y) | n |
|--------------------------------------------------------------------------------------|---|
| Non-recombinant                                                                     |   |
| Hprt^+ + Pgk-1^*/Y                                                                 | 32 |
| Hprt^+ mdx Pgk-1^*/Y                                                               | 33 |
| Hprt^+ + Pgk-1^*/Hprt^+ mdx Pgk-1^*                                                | 27 |
| Hprt^+ mdx Pgk-1^*/Hprt^+ mdx Pgk-1^*                                              | 35 |
| Single recombinant 1, Hprt-mdx                                                     |   |
| Hprt^+ mdx Pgk-1^*/Y                                                               | 3  |
| Hprt^+ + Pgk-1^*/Y                                                                 | 6  |
| Hprt^+ mdx Pgk-1^*/Hprt^+ mdx Pgk-1^*                                              | 1  |
| Hprt^+ + Pgk-1^*/Hprt^+ mdx Pgk-1^*                                               | 3  |
| Single recombinant 2, mdx-Pgk-1                                                    |   |
| Hprt^+ + Pgk-1^*/Y                                                                 | 8  |
| Hprt^+ mdx Pgk-1^*/Y                                                               | 3  |
| Hprt^+ + Pgk-1^*/Hprt^+ mdx Pgk-1^*                                               | 6  |
| Hprt^+ mdx Pgk-1^*/Hprt^+ mdx Pgk-1^*                                              | 4  |
| Double recombinant Hprt-mdx-Pgk-1                                                 |   |
| Hprt^+ + Pgk-1^*/Hprt^+ mdx Pgk-1^*                                               | 1  |
| Total                                                                                | 162 |

Recombination R.F. ± S.E. (%) Confidence interval (95%)

|                           | 14/162 = 8.6 ± 2.2 | 5–3–13-1 |
|---------------------------|-------------------|----------|
| Hprt-mdx                  |                    |          |
| mdx-Pgk-1                 | 22/162 = 13.6 ± 2.7 | 9–4–18-8 |
| Hprt-Pgk-1                | 34/162 = 21.0 ± 3.2 | 15–8–26-9 |

The results of the three-point test with Hprt and Pgk-1 (Table 7) indicated a gene order of Hprt, mdx, Pgk-1. With this order all offspring except one could be explained by the presence of single crossovers. The remaining one would require a double crossover, and with any other order of loci the number of double crossovers would be greater. The recombination frequency between Hprt and mdx is 14/162 = 8.6 ± 2.2% with a 95% confidence interval of 5.3–13.1%. The recombination frequency between mdx and Pgk-1 is 22/162 = 13.6 ± 2.7% with a 95% confidence interval of 9.4–18.8%. The recombination frequency between Hprt and Pgk-1 is 34/162 = 21.0 ± 3.2% with a 95% confidence interval of 15.8–26.9% which does not differ from that previously reported for these two loci (Chapman et al. 1985).
4. Discussion

The two three-point crosses in this report involve six separate loci on the X chromosome. These two crosses provide direct evidence which supports the relative order of X-chromosome genes Hq-G6pd-Ta and Hprt-mdx-Pgk-1. Together with data from two other two-point crosses some indication about the possible ordering of these loci on the X chromosome can be ascertained. A summary of the linkage information involving seven A'-chromosome loci is shown in Fig. 3. The relative positions of G6pd and mdx have not been directly tested and they are assigned provisionally as indicated in the figure. The relative order of Hq-G6pd-mdx is suggested by the recombination frequencies between Hq and G6pd of 51% and between Hq and mdx of 161%. However, this interpretation should be treated with some caution, because the recombination frequency between Hq and Ta of 9.9% in the cross involving G6pd is substantially less than the value of 20.5% previously reported by Isaacscon et al. (1974). Isaacscon et al. (1974) also found a recombination frequency of 24.9 ± 22% between Hq and Mo*; an estimate supported by recent data of Cattanach (1988) who found the Hq-Mo* recombination frequency to be 22.7 ± 1.4%. Possibly the X chromosome with G6pd suppresses recombination in this region, although no evidence of a structural rearrangement could be found in the X chromosome of the stock carrying G6pd (E. P. Evans, personal communication). Our data suggest that G6pd is located about halfway between Hq and Ta and this is in broad agreement with the finding of Martin-DeLeon et al. (1985) which assigned G6pd to the A region by in situ hybridization and with the linkage data of Avner et al. (1987); Brockdorff et al. (1987a,b) using a genomic probe as a marker for G6pd.

Muscular dystrophy, mdx has been located by two- and three-point crosses, using markers from the proximal half of the chromosome. Whereas preliminary work by Bulfield et al. (1984) had positioned mdx to the Hq-Bpa segment, the results of both the two-point and three-point tests in the present study place mdx slightly more distally, to the Str striated/Phk phosphorylase kinase region. Interestingly, Phk is another locus affecting skeletal muscle.

When all the results are considered it is evident that G6pd and mdx must be closely linked. It will be necessary to examine G6pd and mdx in the same cross to verify the most probable order of these loci and the relative distance between these genes.

There appears to be a conserved block of genes in mouse and man containing Hprt and G6pd and whereas in man both Hprt and G6pd are located on the long arm in Xq26-27.3 and Xq28 respectively (Goodfellow et al. 1985), in the mouse the homologous genes are proximal in band A (Lyon et al. 1987b; Martin-DeLeon et al. 1985). The homology between Hprt and HPPRT, and G6pd and G6PD is unequivocal but the human homologue of mdx is less certain. Bulfield et al. (1984) found that mdx showed histological lesions of muscular dystrophy and this raised the possibility that the gene could be homologous with an X-linked muscular dystrophy in man. Two such loci are known in man, EMD, Emery–Dreifuss muscular dystrophy and DMD, Duchenne muscular dystrophy. EMD has been mapped to Xq27 to Xqter, and therefore must be close to G6pd and HPPRT (Hodgson et al. 1986; Yates et al. 1986; Thomas et al. 1986), and DMD has been mapped to Xp21 (Goodfellow et al. 1985). Avner et al. (1987) investigated the localization of five probes on the human and mouse X chromosomes and concluded that the human Xq26 to Xqter region, which includes HPPRT and G6PD, is conserved as a continuous region of the mouse X lying proximal to tabby, Ta. Thus the murine homologue of EMD is predicted to map within this conserved segment. The mouse equivalent of DMD has been located proximal to Ta but distal to G6pd (Brockdorff et al. 1987b; Heilig et al. 1987; Chamberlain et al. 1987). If mdx is proximal to G6pd,
then it may correspond to Emery–Dreifuss muscular dystrophy, but if it is distal to G6pd then it may be homologous with DMD. A direct test of linkage involving G6pd, mdx and other X-linked markers is required to establish the position of mdx. Support for the homology of DMD and mdx has come recently from the finding that the protein dystrophin is absent in DMD-affected individuals and in mdx mice (Hoffman et al. 1987a,b).

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References

Avner, P., Amar, L., Arnaud, D., Hanauer, A. & Cambrou, J. (1987). Detailed ordering of markers localizing to the Xq26-Xqter region of the human X chromosome by the use of an interspecific Mus spretus mouse cross. Proceedings of the National Academy of Sciences U.S.A. 84, 1629–1633.

Brockdorff, N., Fisher, E. C. M., Cavanna, J. S., Lyon, M. F. & Brown, S. D. M. (1987a). Construction of a detailed molecular map of the mouse X chromosome by microcloning and interspecific crosses. EMBO Journal 6, 3291–3297.

Brockdorff, N., Cross, G. S., Cavanna, J. S., Fisher, E. M. C., Lyon, M. F., Davies, K. E. & Brown, S. D. M. (1987b). The mapping of a cDNA from the human X-linked Duchenne muscular dystrophy gene to the mouse X chromosome. Nature 328, 166–168.

Bulfield, G., Siller, W. G., Wight, P. A. L. & Moore, K. J. (1984). X-chromosome-linked muscular dystrophy (mdx) in the mouse. Proceedings of the National Academy of Sciences U.S.A. 81, 1189–1192.

Cattanach, B. M. (1988). Linkage of Hq and Moα*. Mouse News Letter 80, 160.

Chamberlain, J. S., Grant, S. G., Reeves, A. A., Mullins, L. J., Stephenson, D. A., Hoffman, E. P., Monaco, A. P., Kunkel, L. M., Caskey, C. T. and Chapman, V. M. (1987). Regional localization of the murine Duchenne muscular dystrophy gene on the mouse X chromosome (1987). Somatic Cell and Molecular Genetics 13, 671–678.

Chapman, V. M. & Shows, T. B. (1976). Somatic cell genetics. Mouse News Letter 71, 37.

Charles, D. J. & Pretsch, W. (1984b). A mouse mutant deficient in erythrocyte glucose-6-phosphate dehydrogenase after paternal ethynitrosourea treatment. Genetics 107, s19.

Charles, D. J. & Pretsch, W. (1986). Enzyme-activity mutations detected in mice after paternal fractionated irradiation. Mutation Research 160, 243–248.

Epstein, C. J. (1969). Mammalian oocytes: X chromosome activity. Science 163, 1078–1079.

Goodfellow, P. N., Davies, K. E. & Ropers, H.-H. (1985). Report of the committee on the genetic constitution of the X and Y chromosomes. Eighth International Workshop on Human Gene Mapping. Cytogenetics and Cell Genetics 40, 296–352.

Heilig, R., Lemaire, C., Mandel, J.-L., Dandolo, L., Amar, L. & Avner, P. (1987). Localization of the region homologous to the Duchenne muscular dystrophy locus on the mouse X chromosome. Nature 328, 168–170.

Hodgson, S., Boswinkel, E., Cole, C., Walker, A., Dubowitz, V., Granata, C., Merlini, L. & Bobrow, M. (1986). A link study of Emery–Dreifuss muscular dystrophy. Human Genetics 74, 409–416.

Hoffman, E. P., Brown, Jr., R. H. & Kunkel, L. M. (1987a). Dystrophin: the protein product of the Duchenne muscular dystrophy locus. Cell 51, 919–928.

Hoffman, E. P., Knudson, C. M., Campbell, K. P. & Kunkel, L. M. (1987b). Subcellular fractionation of dystrophin to the tracks of skeletal muscle. Nature 330, 754–758.

Isaacson, J. H., Stewart, J. & Falconer, D. S. (1974). Private communication. Mouse News Letter 50, 33.

Lyons, M. F. (1987a). Mouse chromosome atlas. Mouse News Letter 78, 12–33.

Lyons, M. F., Zentthon, J., Burtenshaw, M. D. & Evans, E. P. (1987b). Localization of the HpRT locus by in situ hybridization and distribution of loci on the mouse X-chromosome. Cytogenetics and Cell Genetics 44, 163–166.

Martín-DeLeon, P. A., Wolf, S. F., Persico, G., Toniolo, D., Martini, G. & Migeon, B. R. (1985). Localization of glucose-6-phosphate dehydrogenase in mouse and man by in situ hybridization: evidence for a single locus and transposition of homologous X-linked genes. Cytogenetics and Cell Genetics 39, 87–92.

Peters, J. & Ball, S. T. (1985). Private communication. Mouse News Letter 73, 17–18.

Pretsch, W., Charles, D. J. & Merkle, S. (1988). X-linked glucose-6-phosphate dehydrogenase deficiency in Mus musculus. Biochemical Genetics; (in the press).

Thomas, N. S. T., Williams, H., Elsas, L. J., Hopkins, L. C., Sarfarazi, M. & Harper, P. S. (1986). Localization of the gene for Emery–Dreifuss muscular dystrophy to the distal long arm of the X chromosome. Journal of Medical Genetics 23, 596–598.

Yates, J. R. W., Affara, N. A., Jamieson, D. M., Ferguson-Smith, M., Hausmanowa-Petrusewicz, I., Zaremba, J., Borkowska, J., Johnston, A. W. & Kelly, K. (1986). Emery-Dreifuss muscular dystrophy: localisation to Xq27.3-qter confirmed by linkage to the factor VIII gene. Journal of Medical Genetics 23, 587–590.