The sex chromosome association (*Sxa*) gene is located on the X-chromosome in mice

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ABSTRACT

The genetic factor “*Sxa*” controlling the end-to-end association of the sex chromosome in mice is linked closely (R.V.=4.6%) to *Crn* (cream), which is located near the distal end of the X chromosome.

1. INTRODUCTION

Since the high frequency of X-Y dissociation (50–90%) was first found in primary spermatocytes of inter-subspecies hybrid of mouse (Imai et al., 1981), a series of cytogenetic analyses of the phenomenon have been achieved (Matsuda et al., 1982, 1983). We suggested that the X-Y dissociation is controlled by a genetic factor (*Sxa*) which is responsible for the end-to-end association of the sex chromosomes. For detailed nomenclature of *Sxa* see Green (1989). There are at least two alleles, *Sxa^a* and *Sxa^b*. *Sxa^a* is found in laboratory mouse strains and *Mus musculus domesticus*, while *Sxa^b* is characteristic of Japanese wild mice (*M. m. molossinus*). The remarkable X-Y dissociation (>50%) appears only in the heterozygous genotype (*Sxa^a/Sxa^b*), but it is less than 20% in homozygous genotypes (*Sxa^a/Sxa^a* or *Sxa^b/Sxa^b*). We also suggested that *Sxa* is located on the common part of the X and Y chromosomes (presumably near the distal end). To confirm our assumption, the present study attempted a linkage test of *Sxa* and *Crn*.

2. MATERIALS AND METHODS

We used MOA inbred strain and a mutant stock having *Crn* (cream) near the distal end of the X-chromosome. MOA strain was established by Kondo (1979) from Japanese wild mouse (*Mus musculus molossinus*), which carries *Sxa^b* (Matsuda et al., 1983). The *Crn* mutant (Searle and Beechy, 1977) in an albino background (*c/c*) was obtained from MRC in 1985 by courtesy of Dr. M. F. Lyon. The genetic background of *Crn* mouse seems to be extremely heterogeneous, because it has been crossed with mice of C3H/HeH, 101/H and then with non-agouti albino inbred, JU/FaCt (Cattanach, personal communication). *Crn*

was a sole marker gene to test *Sxa* linkage having been available at that time, when it was located at the most distal end on the X chromosome.

Chromosome analyses of MOA and Crm mice were carried out with the right testis of 8-wk old males using the air-drying technique described by Imai et al.

Fig. 1. Mating scheme for the linkage test between *Crm* and *Sxa*. c; albino gene located on chromosome 7. +; agouti (the wild-type coat colour). Crm; cream. *Sxa*; a genetic factor controlling the end-to-end association of the sex chromosome. Solid and open columns indicate X and Y chromosomes of the Crm mutant stock and MOA strain, respectively. Inset; F₁ males, which have X//Y=55.8±8.6%. The X//Y values of MOA and Crm males were 37.0% and 6.8%, respectively. Numerals are the number of mice observed. The frequency of X-Y dissociation in N₂ is represented in parentheses.

(1981). The frequency of X-Y dissociation in each individual was estimated from 100 spermatocytes at metaphase I. After cytological examination, a male MOA was mated with a Crm female. Twenty female F_1 progeny were backcrossed to a Crm male. At the first backcross generation (N_2), three types of male progeny were segregated according to coat colour (agouti (wild-type), cream, and albino), in which cream and albino males were examined cytologically. A mating scheme of the present linkage test is summarized in Fig. 1.

3. RESULTS AND DISCUSSION

The frequency of X-Y dissociation (represented as X//Y %) of MOA, Crm, and their hybrid (Crm $\times$ MOA) F_1 males was 37.0% (one male), $6.8\pm2.5\%$ (8 males) (Fig. 2A), and $55.5\pm8.6\%$ (40 males) (Fig. 2B), respectively. In connection with this, previous experiments with BALB/c and MOA showed somewhat different dissociation patterns, i.e., MOA ($26.8\pm4.8\%$), BALB/c ($12.5\pm4.4\%$), and (BALB/c $\times$ MOA) F_1 ($75.3\pm5.5\%$) (Matsuda et al., 1983). The X//Y value of MOA in the present experiment was slightly higher than that obtained before, while (Crm $\times$ MOA) F_1 showed a significantly lower value than (BALB/c $\times$ MOA) F_1 . Such differences may have partly resulted from the heterogeneity of the genetic background of MOA and especially Crm mice. The pattern of X-Y dissociation of MOA, Crm and their hybrids seems to be that of Type II found in DBA/2J and DDK rather than Type I which is characteristic of inter-subspecies hybrids (Matsuda et al., 1982). In Type II, X//Y is about 30% in the homozygous condition and increases up to about 50% in inter-strain hybrids (C57BL/6J $\times$ DBA/2J or DDK), though the genetic mechanism is not yet known.

To simplify the linkage test, we defined those males showing X//Y<30% as Low X//Y males and those with X//Y $\geq$ 30% as High X//Y, and also assumed *Sxa* alleles of Crm and MOA as *Sxa*^a and *Sxa*^b, respectively. Note that in Type I the borderline of Low X//Y and High X//Y is 50% (Matuda et al., 1983). With the present criteria, (Crm $\times$ MOA) F_1 and MOA are grouped as High X//Y, and Crm as Low X//Y (Fig. 2A). The MOA male used in the present experiment may have different types of *Sxa* despite the inbred strain established. It does not affect, however, our present argument, because we examined in this study the cross-over value between *Crm* and *Sxa* of the X chromosomes (Fig. 1).

Among the total of 104 N_2 males obtained, three types of progeny were segregated according to coat color as follows; agouti (wild-type) 88, cream 51, and albino 53. We examined the X-Y dissociation of cream and albino males. Most of the cream males (49) were Low X//Y ($8.8\pm4.7\%$), but 2 males were obviously High X//Y ($41.5\pm4.5\%$) in the present classification system (Fig. 2C). In the same manner, among albino mice 50 males were identified as High X//Y ($56.2\pm11.5\%$) while 3 males were Low X//Y ($16.0\pm2.9\%$) (Fig. 2C). We have temporarily characterized these mice according to their coat colour and X//Y class

Fig. 2. Results of the linkage test between *Crm* and *Sxa* genes. A. Parent strains. Cream strain (*Crm*, open column). MOA with agouti coat color (solid column). B. F₁ hybrid with agouti coat color. (MOA × *Crm*)F₁. C. N₂ progeny. [(MOA × *Crm*)F₁ × *Crm*]N₂. Low X//Y and High X//Y are defined respectively as X//Y < 30% and X//Y ≥ 30% by X-Y dissociation frequency (broken lines). Recombinants at N₂ are shown by open or solid circles.

as (Low X//Y, *Crm*), (High X//Y, Alb), (High X//Y, *Crm*), and (Low X//Y, Alb). The former two are parent types and the latter two are recombinants (Fig. 1). Thus, we conclude that *Sxa* is linked closely with *Crm*, and that the recombination value between them is R.V. = 4.6%.

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