

Letter to the Editor

Does Sex of the Offspring Influence Transmission Ratio?

Transmission ratio distortion (TRD) is an interesting exception to mendelism that has been most convincingly demonstrated in the mouse in studies of *t*-haplotypes (BENNETT 1975; BENNETT, ALTON and ARTZT 1983; LYON 1984, 1986; SILVER 1985). Recently, JENKINS, COPELAND and colleagues have reported evidence of TRD in interspecific backcross mice (SIRACUSA *et al.* 1989, 1991; CECI *et al.* 1989; JUSTICE *et al.* 1990). I am most interested in their reports of TRD involving chromosome 2 because we have seen TRD of this chromosome in crosses of laboratory mice (D. B. LIND and P. E. NEUMANN, unpublished results) and because they have reported differences in TRD associated with the sex of the offspring (SIRACUSA *et al.* 1991).

In a set of four backcrosses in our laboratory involving C57BL/6J mice and F₁ hybrids from crosses with linkage stocks obtained from The Jackson Laboratory (Bar Harbor, Maine), more than half of the offspring were nonagouti (*a/a*) (see Table 1). In three of the four backcrosses, 62.4% (weighted mean) of the offspring were nonagouti. One of the backcrosses was not significantly different from the expected 1:1, but it is significantly different from the TRD seen in the other backcrosses ($\chi^2 = 9.8$, 1 d.f.). These results support the conclusion of Siracusa *et al.* (1991) that a locus (or loci) on chromosome 2 is involved in TRD of a region of that chromosome. It is reasonable to speculate that the same locus (or loci) may be responsible for the TRD in the interspecific backcross and the three intraspecific backcrosses because the transmission ratios associated with the tightly linked *a* and *Emv-15* loci were virtually identical. However, it is interesting to note that while the proportion of alleles derived from B6 is reduced in the interspecific backcross, we found an excess in backcrosses with other laboratory mice. This is reminiscent of the ordering of a series of *t*-haplotypes with respect to TRD.

The effect of the sex of the parent on TRD has been well documented in the case of various *t*-haplotypes, however, the recent report of differences in TRD associated with the sex of backcross offspring is less compelling. A simpler model cannot be ruled out. This model assumes a single locus (or a cluster of loci) on chromosome 2 is involved in the TRD effect. This locus probably maps close to *Bmp-2a* because this marker locus is associated with the greatest TRD. For the purposes of this model, we will assume that there is no recombination between the TRD locus and *Bmp-*

TABLE 1

Transmission ratio distortion in four sets of intraspecific backcrosses of reciprocal F₁ hybrids to C57BL/6J inbred mice

Cross	F ₁ parent	N	a	a/N	χ^2
STX/Le	Male	105	66	0.629	6.943 ($p = 0.008$)
MWT/Le	Female	85	39	0.459	0.576
ROP/GnLe	Male	109	67	0.615	5.734 ($p = 0.017$)
ROP/GnLe	Female	73	46	0.630	4.945 ($p = 0.026$)
Total		372	218	0.586	11.011 ($p = 0.0009$)

Note: Data from D. B. LIND and P. E. NEUMANN (unpublished). Cross = the linkage stock crossed with C57BL/6J mice to produce the heterozygous parent; F₁ parent = sex of the heterozygous parent; N = sample size; a = number of nonagouti (*a/a*) offspring; P = proportion of nonagouti offspring; χ^2 values have one degree of freedom.

2*a* in the interspecific backcross. Therefore, transmission ratio (*t*) associated with a marker locus is linearly related to the recombination frequency (*r*) between that marker locus and the TRD and *Bmp-2a* loci;

$$t = 0.658 - 0.316r.$$

The TRD associated with each of the marker loci in males, females and combined samples does not differ significantly from that predicted by this model (see Table 2). The sex differences found by Siracusa *et al.* are partially accounted for by differences in recombination frequency in male and female offspring that probably represent a statistical fluctuation. If the sex of offspring influences transmission ratio, analysis of a larger sample is required to demonstrate it.

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TABLE 2

Chi-squared analysis of linear model of transmission ratio distortion as a function of recombination frequency

Locus	Total (N = 117)				Females (N = 49)				Males (N = 68)			
	r	t	Exp	χ^2	r	t	Exp	χ^2	r	t	Exp	χ^2
<i>Vim</i>	0.419	0.479	0.526	1.04	0.286	0.592	0.568	0.12	0.515	0.397	0.495	2.64
<i>Spna</i>	0.393	0.487	0.534	1.02	0.245	0.592	0.581	0.03	0.50	0.412	0.50	2.12
<i>Abl</i>	0.368	0.530	0.542	0.07	0.245	0.633	0.581	0.54	0.456	0.456	0.514	0.90
<i>Hc</i>	0.342	0.521	0.550	0.38	0.224	0.612	0.587	0.12	0.426	0.456	0.523	1.25
<i>His-1</i>	0.291	0.590	0.566	0.27	0.224	0.653	0.587	0.51	0.338	0.544	0.551	0.01
<i>Neb</i>	0.273	0.607	0.572	0.59	0.224	0.653	0.587	0.51	0.309	0.574	0.560	0.05
<i>Hox-4.1</i>	0.188	0.624	0.599	0.32	0.163	0.673	0.606	0.93	0.206	0.588	0.593	0.01
<i>D2Hgu1</i>	0.137	0.607	0.615	0.03	0.143	0.653	0.613	0.34	0.132	0.574	0.616	0.52
<i>Fshb</i>	0.111	0.615	0.623	0.03	0.122	0.673	0.619	0.38	0.103	0.574	0.625	0.77
<i>Actc-1</i>	0.085	0.624	0.631	0.02	0.102	0.653	0.626	0.13	0.074	0.603	0.635	0.31
<i>B2m</i>	0.043	0.632	0.644	0.07	0.061	0.653	0.639	0.04	0.029	0.618	0.649	0.28
<i>Bmp-2a</i>	0.00	0.658	0.658		0.00	0.673	0.658	0.06	0.00	0.647	0.658	0.03
<i>Pax-1</i>	0.06	0.632	0.639	0.02	0.02	0.653	0.651	0.00	0.088	0.618	0.630	0.04
<i>Hck-1</i>	0.128	0.632	0.618	0.12	0.143	0.612	0.613	0.00	0.118	0.647	0.621	0.20
<i>Emv-15</i>	0.128	0.632	0.618	0.12	0.143	0.612	0.613	0.00	0.118	0.647	0.621	0.20
<i>Ada</i>	0.154	0.641	0.609	0.49	0.163	0.592	0.606	0.04	0.147	0.676	0.612	1.20
<i>Pck-1</i>	0.231	0.581	0.585	0.01	0.286	0.469	0.568	1.92	0.191	0.662	0.598	1.18

Note: Data from SIRACUSA *et al.* (1991).

r = recombination frequency between marker locus and *Bmp-2a*; t = transmission ratio, the proportion of offspring with the allele derived from *M. spretus*; Exp = the expected value of t based on the linear regression $t = 0.658 - 0.316r$; χ^2 values have one degree of freedom.

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