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Occurrences and linkage relations of the mutant 'extra-toes' in the mouse

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The name *extra-toes*, symbol *Xt*, has been given to a new autosomal dominant mutant gene affecting the skeletal system of the mouse, *Mus musculus* L. The first mutant allele to be found arose spontaneously in the control series of a radiation experiment (Lyon *et al.*, 1964), whereas several later reoccurrences were probably radiation-induced (Table 1).

Table 1. *Alleles of* extra-toes, Xt, *found at Harwell*

Allele	Origin	Inducing agent	Evidence for allelism with original allele
Xt	Spontaneous	—	—
Xt^{2H}	Induced	2 × 600 r. X-rays to spermatogonia	Similar homozygote, compound, and linkage relations
Xt^{3H} (= *Bph*)	Induced	214 r. neutrons + 93 r. γ-rays to spermatogonia	Johnson (1967)
Xt^{4H}	Induced	600 r. X-rays to spermatogonia	Similar compound and linkage relations
Xt^{5H}	Induced	2 × 500 r. X-rays to spermatogonia	Similar homozygote, compound, and linkage relations
Xt^{6H}	Induced	2 × 500 r. X-rays to spermatogonia	Similar homozygote
Xt^{7H}	Spontaneous	—	Similar homozygote

A detailed description of the morphology and embryology of the first allele is given by Johnson (1967). Briefly the effects are, in the heterozygote, preaxial polydactyly of the hind-feet, sometimes with shortening and twisting of the preaxial digits of the fore-feet and, in the homozygote, gross polydactyly of all feet, combined with cranioschisis, so that the homozygotes die at or before birth. Data from linkage backcrosses (Table 3) illustrate the fact that the gene shows good viability and penetrance in the heterozygote. However, care is needed in classification, since in some animals the extra toe may be represented by nothing more than a slight swelling on the preaxial side at the base of an otherwise normal first hind toe. Moreover, normal overlapping has occasionally been found in crosses on to other genetic backgrounds.

The alleles Xt^{2H}, Xt^{5H} and Xt^{6H} were all indistinguishable from *Xt* in their effects in both heterozygote and homozygote. The fourth allele, Xt^{4H}, was similar to *Xt* in the heterozygote, but in the homozygote was lethal in the pre-implantation period, there being a reduced number of implants in crosses of $Xt^{4H}+ \times Xt^{4H}+$ (Table 2). The remaining allele

Xt^{3H}, previously called brachyphalangy, *Bph*, by Batchelor *et al.* (1965), had similar but distinguishable effects in both heterozygote and homozygote (Johnson, 1967). In the heterozygote the preaxial digits of the fore-feet were more markedly shortened than in *Xt*, and on the hind-feet, instead of a separate extra digital rudiment, there was shortening and thickening of the hallux, sometimes with a double claw or syndactylous extra phalanges.

Table 2. *Evidence from dissections of pregnant females for pre-implantation death of homozygous* Xt^{4H}

Cross ♀	Cross ♂	No. of females	CL	I	L	D	M	I/CL %	L/I %
Xt^{4H}+	++	17	159	123	87	14	22	77·4	70·7
++	Xt^{4H}+	11	138	110	93	5	12	79·7	84·5
Xt^{4H}+	Xt^{4H}+	43	417	260	191	13	56	62·4	73·5

(CL = corpora lutea; I = implants; L = live, normal embryos; D = dead or abnormal; M = moles).

The first six alleles were all derived on the paternal side from a (C3H/HeH × 101/H) F_1 hybrid stock and Xt^{7H} arose in an unrelated stock of random bred mice carrying Cattanach's translocation and extreme dilution, c^e. The original individuals carrying *Xt* and Xt^{7H} were missed but it is known that Xt^{2H}, Xt^{3H}, Xt^{4H} and Xt^{6H} arose as single individuals in large sibships and Xt^{5H} as a cluster of three individuals in different litters of a large sibship.

Table 3. *Phenotypes of offspring of three-point backcrosses of* +Xt+/cr+f *and of* cr Xt+/++pe *heterozygotes*

	Allele and sex of heterozygote			
	Xt		Xt^{4H}	
Offspring of +*Xt*+/*cr*+*f*	♀	♂	♀	♂
cr + *f*	34	71	26	28
+ *Xt* +	49	120	26	31
cr Xt +	0	1	1	0
+ + *f*	0	0	2	0
cr + +	10	17	8	5
+ *Xt f*	6	15	2	5
cr Xt f	0	0	0	0
+ + +	0	1	0	0
Total	99	225	65	69

	Xt	
Offspring of *cr Xt*+/++*pe*	♀	♂
cr Xt +	69	10
+ + *pe*	78	6
cr + *pe*	2	0
+ *Xt* +	3	0
cr Xt pe	49	4
+ + +	68	7
cr + +	0	0
+ *Xt pe*	0	0
	269	27

Single-factor segregation	*Xt*	+
+ *Xt*+/*cr*+*f*	191	133
+ Xt^{4H}+/*cr*+*f*	65	69
cr Xt+/++*pe*	135	161
Total	391	363

Linkage tests showed that *Xt* was in linkage group XIV, closely linked to crinkled, *cr*, and loosely linked to flexed-tail, *f*, and to pearl, *pe*, a gene that was not previously known to be in this linkage group. Three-point linkage backcrosses with *cr*, *Xt* and *f* and with *cr*, *Xt* and *pe* showed *Xt* to be the middle locus of each group (Table 3) with the corollary that *f* and *pe* must be on the same side of *cr*. This was confirmed by three-point intercrosses of

cr f+/++*pe*, in which *f* and *pe* proved to be closely linked, there being only one *pepe ff* animal among 396 offspring. Two-point backcrosses showed *Xt* to be nearer to *f* than to *pe*. Therefore the order of loci must be

$$cr - Xt - f - pe$$

with *pe* a new end-marker in this group. The estimated recombination fractions are shown in Table 4. (In the three-point intercrosses of *cr*, *f* and *pe* reduced viability of *f* and *cr* made estimation of the *f* − *pe* recombination not worthwhile.)

Table 4. *Recombinations between* cr, Xt, f *and* pe *in male and female heterozygotes. Combined data from two and three-point backcrosses*

	Recombination			
	Female		Male	
Heterozygote	No.	%	No.	%
cr +/+ *Xt* *cr Xt*/++	3/164 5/269	1·85 ± 0·65	2/294 0/27	0·62 ± 0·44
Xt +/+ *f* *Xt f*/++	65/284 4/20	22·7 ± 2·40	62/363 31/122	19·2 ± 1·79
Xt +/+ *pe* *Xt pe*/++	179/423 35/78	42·7 ± 2·21	63/183 40/159	30·1 ± 2·48

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