

The genetics of tasting in mice VII. Glycine revisited, and the chromosomal location of *Sac* and *Soa*

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Summary

Previous work which appeared to show that some strains of mice taste glycine solutions as bitter has been found to be in error. The bitterness came from copper glycinate which formed in the brass drinking spouts. Taste testing with copper glycinate shows that the genetical data identifying the gene *Glb* are still valid. The close linkage of *Glb* and *Rua* has been confirmed. Most strains of mice prefer glycine solution to water, presumably because the glycine tastes sweet. The degree of preference for glycine is correlated with the degree of preference for other sweet substances such as saccharin or acesulfame. The gene *dpa* appears not to be involved.

The sweetness tasting gene *Sac* has been mapped to chromosome 4 at 8.1 ± 3.4 cM distal to *Nppa* (formerly *Pnd*). The bitterness tasting gene *Soa* is very closely linked to *Prp* on chromosome 6 (no recombinants among 67 backcross progeny). It is suggested that the sweetness and bitterness tasting genes have descended from a common ancestral tasting gene which existed before the tetraploidization of the genome which took place in early vertebrate evolution.

1. Introduction

In a previous paper in this series (Lush & Holland, 1988) it was stated that some strains of mice taste glycine solutions as bitter. The apparatus which was used in these experiments delivered the solutions to the mice through drinking spouts which were made of brass. Although the external surface of each spout was chromium-plated the inner surface was not, and it was subsequently found that the glycine in the solution was able to react with the copper component of the brass, thus producing a solution of copper glycinate which is pale blue. As soon as this was noticed the brass spouts were replaced by glass spouts, with the result that the blue colour was no longer present. Also, after the change to glass spouts, none of the mouse strains tasted glycine as bitter. This seemed to show that the bitterness was due to copper glycinate and not to glycine.

Nevertheless, the published results which had been obtained using the brass spouts were remarkably consistent and were used to show the segregation of a gene, *Glb*, which determines the ability to taste the bitterness of the 'glycine' solution. If the mice were in fact tasting the bitterness of copper glycinate, as seems

to be the case, the genetic data may still be valid even though they refer to copper glycinate and not to glycine. We have therefore prepared copper glycinate and used it to test the same strains of mice to see if the existence of the *Glb* gene can be confirmed. The results are presented in this paper.

Glycine tastes sweet to several strains of mice (Lush & Holland, 1988) but in previous experiments it was impossible to study the sweetness without the risk of interference from the bitterness which was unwittingly introduced as described above. We have now retested the same strains of mice with glycine and confirmed that there is indeed variation between strains in their ability to taste the sweetness of glycine. Probably more than one gene influences this variation.

The gene *Sac* has a major effect on the ability of a mouse to taste sweet substances (Lush, 1989). The strain distribution pattern (SDP) of *Sac* alleles among 21 BXD RI strains is very similar to the SDPs of two genes mapped near the telomeric end of chromosome 4. The SDPs of all three genes are shown in Table 1 where it can be seen that the SDP of *Sac* differs from those of the other loci by two RI strains in each case. This suggests that *Sac* lies between the other two genes (as shown in Table 1) although the order of *D4Smh6b* and *Tel4q* relative to the centromere is uncertain. We report here the result of a three-point

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Table 1. A comparison of the D4Smh6b, Sac and Tel4q distribution patterns in the BXD RI strains

Gene	BXD RI strains																				
	1	2	5	6	8	9	11	12	15	16	18	19	22	24	25	27	28	29	30	31	32
<i>D4Smh6b</i> †	D	D	B	B	D	B	B	D	B	D	D	n.t.	D	B	B	B	D	B	D	B	D
<i>Sac</i> †	D	D	B	B	D	D	B	D	B	D	D	B	D	B	B	D	D	B	D	B	D
<i>Tel4q</i> *	D	D	B	B	D	D	B	D	X	D	n.t.	B	X	B	B	D	D	B	D	B	D

* Data from Elliott & Yen (1991).

† Data from Lush (1989) with the addition of BXD9.

‡ Data from Hearne *et al.* (1991).

n.t. Not tested.

cross designed to confirm this chromosomal position of *Sac*.

The gene *Soa* determines the ability of a mouse to taste the bitterness of a number of acetylated sugars, of which sucrose octaacetate (SOA) is one. *Soa* also affects the ability to taste the bitterness of strychnine (Lush, 1982, 1991). Other bitterness-tasting genes i.e. *Cyx*, *Qui*, *Rua* and *Glb* form a cluster on chromosome 6. This cluster includes *Prp* which codes for a salivary proline-rich protein (Lush & Holland, 1988; Azen *et al.* 1989). *Soa* has recently been mapped to the same cluster of genes on the basis that no recombination has been found between *Soa* and *Prp*, or between *Prp* and *Rua*, in a number of RI and congenic strains (Capeless *et al.* 1990, 1992; Azen, 1991). In this paper we confirm the close linkage of *Soa* and *Prp*.

We believe that our results throw light on homologies between mouse chromosome 4 and 6.

2. Materials and Methods

The strains of mice are those which were used previously (Lush & Holland, 1988), and they are listed in Table 2. In addition, a strain containing the gene crooked tail, *Cd*, was used. *Cd*, is a dominant gene which produces a crooked tail, but has the disadvantage of incomplete penetrance in heterozygotes (Morgan, 1954). It is effectively lethal in homozygotes, so the *Cd* strain is maintained by breeding from heterozygotes. There is no evidence that *Cd*/+ mice are less viable, before or after birth, than are their normal littermates.

The taste testing procedure has been described in detail elsewhere (Lush, 1984). Very briefly, the mice could drink from two spouts. One of these supplied the tastant solution and the other supplied the control solution which was usually distilled water. The spouts and their contents were changed around in the course of the 4-day experiment in such a way as to compensate for any preference the mice might have for drinking from a particular spout or a particular spout position. Each day the tastant consumed by the mouse, or mice, in a cage was expressed as a percentage of the total

fluid which they drank that day, and the final result was the mean of the results over the 4 days.

Glycine, raffinose undecaacetate (RUA) and saccharin (sodium salt) came from Sigma and were of the highest purity available. Acesulfame was a gift from Hoechst U.K. Ltd. Glycine and saccharin were dissolved in distilled water. RUA was dissolved in a small quantity of ethanol before being diluted with distilled water (Lush, 1986). The control solution contained the same amount of ethanol.

Copper (II) glycinate, $\text{Cu}(\text{NH}_2\text{CH}_2\text{COO})_2$ was prepared as follows. One mole of NaOH pellets was added to an aqueous solution of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.5 mole). A voluminous blue precipitate formed and then rapidly darkened, converting to black CuO which was filtered off. The CuO precipitate was washed with distilled water and left to dry. The yield was almost quantitative. The CuO was suspended in distilled water and 1.0 mole of glycine was added with stirring. A thick precipitate of copper glycinate was thrown down. This was redissolved by the addition of distilled water to give a final concentration of 25 mM. This stock solution was stored at 4 °C. On storage, a slight precipitate may form but this redissolves if the solution is gently heated to 40–50 °C. The stock solution was diluted with distilled water to give the concentration required for the experiment. The copper salt of L-valine was made by the same method.

For DNA preparation, tissue samples were incubated at 55 °C overnight in 0.5 ml TNES containing proteinase K. 1 ml of TNES contains: 50 μl , 1.0 M-Tris, pH 7.5; 200 μl , 2.0 M-NaCl; 200 μl , 0.5 M-EDTA; 50 μl , 10% SDS; 500 μl , H_2O . The NaCl concentration was adjusted to 1.5 M by adding an equal volume of 2.6 M-NaCl. The tubes were shaken vigorously for 15 s and centrifuged at 12000 $\times g$ for 5 min. Supernatants were transferred to clean tubes and mixed with an equal volume of ethanol. DNA was spooled out and dissolved in Tris-EDTA buffer, pH 7.5.

The PCR primers have been described for *Lck* (Todd *et al.* 1991), *Nppa* (Wiseman *et al.* 1994), *D4Smh6b* (Hearne *et al.* 1991) and *Prp* (*D6Prp*) (Love *et al.* 1990). Radiolabelled products for *D4Smh6b* and

Table 2. Consumption of copper glycinate, copper valinate and glycine by mice from twenty-three strains. Each cage contained up to 4 mice

Strain	Tastant					
	Copper glycinate (1.0 mM)		Copper valinate (0.5 mM)		Glycine (200 mM)	
	Cages tested	Mean tastant consumed (%)	Cages tested	Mean tastant consumed (%)	Cages tested	Mean tastant consumed (%)
TO	6	65	4	57	4	79
129/Sv	6	60	8	45	6	55
STS	4	32	.	.	4	88
129/Rr	4	49	.	.	4	80
C57BL/6By	4	39	.	.	4	81
C57L	4	48	.	.	4	92
C57BL/6Ty	4	33	4	20	4	93
IS/Cam	4	35	.	.	4	81
NMRI	4	39	4	42	4	66
DBA/1	4	12	.	.	4	76
Schneider	4	13	2	14	4	83
CE	4	3	.	.	4	68
A/J	4	4	.	.	4	76
CBA	4	3	.	.	10	70
AKR	4	9	.	.	4	77
SEA	4	3	.	.	3	85
SWR	4	4	.	.	4	81
A2G	4	3	.	.	5	89
ST/bJ	4	2	.	.	n.t.	n.t.
C3H/He	4	2	.	.	4	85
DBA/2Ty	4	14	2	12	4	85
BALB/cBy	4	11	2	10	6	71
BALB/cAm	4	6	.	.	8	40

n.t. = Not tested.

D6Prp were resolved on acrylamide gels as described by Dietrich *et al.* (1992). Reaction products for *Lck* and *Nppa* were digested with HaeIII and PvuII respectively, and resolved on 2% agarose gels.

Correlations were calculated as the non-parametric Spearman rank correlation coefficient r_s (Siegel, 1956).

3. Results

(i) Copper glycinate and copper valinate

Twenty-three strains were tested with 1.0 mM copper glycinate as tastant. The results are shown in Table 2. When these data were plotted against the previously-published results (from the same strains but using glycine with brass drinking-spouts) it was found that there is an excellent correlation ($r_s = 0.77$; $P < 0.01$) between the two sets of data (see Fig. 1). Nine strains were 'non-tasters' in both sets of data and the other 14 strains were 'tasters' in both sets of data. This is strong evidence that copper glycinate is the substance which is being tasted in both situations.

In the previous paper (Lush & Holland, 1988) a backcross was made to demonstrate segregation of the 'taster' and 'non-taster' alleles of the *Glb* gene; denoted by *Glb*^a and *Glb*^b respectively. This cross,

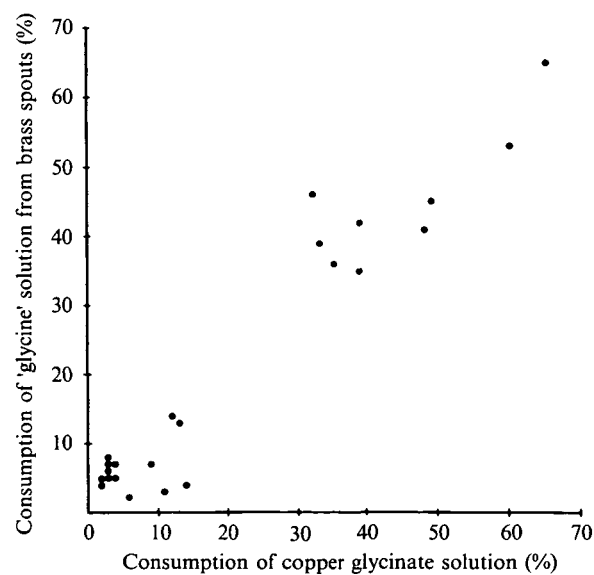


Fig. 1. Consumption of copper glycinate (1 mM) and 'glycine' (10 mM) by 23 strains of mice. The copper glycinate data are taken from Table 1. The 'glycine' data come from Lush & Holland (1988) when brass drinking-spouts were used.

which was 129/Sv \times F₁ (BALB/cBy \times 129/Sv), was therefore repeated, and 34 progeny were tested with 1.0 mM copper glycinate. The progeny were also tested

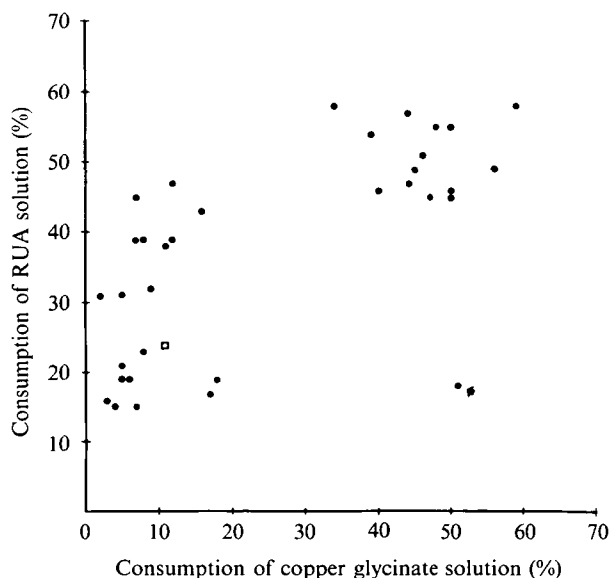


Fig. 2. Consumption of copper glycinate (1 mM) and RUA (0.4 mM) by the 34 progeny of the backcross 129/Sv \times F₁ (BALB/cBy \times 129/Sv). □, mean of three F₁ mice. ●, the 34 progeny. The mouse indicated by the arrow had a recombinant phenotype.

with raffinose undecaacetate (RUA) to check the linkage of *Glb* with *Rua*. This linkage was proposed on the basis of the very similar strain distribution patterns of *Glb* and *Rua* in the BXD RI strains (Lush & Holland, 1988). The results of the present cross are shown in Fig. 2. The F₁ mice were tasters of both copper glycinate and also RUA thus indicating dominance by the taster alleles of both genes. With respect to copper glycinate, the progeny of the backcross clearly separated in 19 tasters (mean = 8.0%) and 15 non-tasters (mean = 46.8%). This is not significantly different from the expected 1:1 ratio. The same classification was obtained when the same mice were tested with glycine using brass drinking-spouts (unpublished data).

With respect to RUA the segregation is not so clear. Evidence for the existence of the *Rua* gene was based on its segregation among RI strains. Overlapping between the phenotypes of homozygotes and heterozygotes made it impossible to confirm this by means of a conventional backcross (Lush, 1986). The same problem is evident in the RUA data shown in Fig. 2. If *Glb* and *Rua* are linked, and if the taster alleles of both genes showed complete dominance, then the non-recombinant progeny of this backcross would be either tasters of both tastants (like the F₁ parent) or non-tasters of both tastants. The recombinant progeny would be tasters of one tastant and non-tasters of the other. Clear evidence of linkage does occur among the copper glycinate non-tasters, where there are 14 non-recombinant progeny and one (arrowed) recombinant. This recombinant mouse was tested three times with RUA and three times with copper glycinate and its phenotype is therefore reasonably certain. The data from these 15 backcross mice gives a genetic distance

between *Glb* and *Rua* of 6.7 ± 6.4 cM, which agrees with the estimate of 0.91 cM (95% confidence limits 0.02–6.05) based on the RI strain data (Lush & Holland, 1988). In view of this evidence of linkage, most of the 19 backcross progeny which are copper glycinate tasters are probably also genotypically RUA tasters (*Rua^a/Rua^b*) although the lack of complete dominance of the taster allele (*Rua^a*) means that it is impossible to identify any recombinant individuals among them. Nevertheless, the data as a whole do support the existence of tight linkage between *Glb* and *Rua*.

Seven strains were tested with 0.5 mM copper valinate to see if the taste depends on the nature of the amino acid. The data, given in Table 2, show that there is a good correlation ($r_s = 0.96$; $P < 0.01$) between the results with copper glycinate and those with copper valinate. This indicates that the presence of a short aliphatic side-chain does not affect the nature of the taste.

(ii) Glycine

After some initial experiments, a concentration of 200 mM was chosen to test all the strains with glycine. The results are shown in Table 2. Nearly all the strains prefer glycine to water, presumably because the glycine tastes sweet to them. There is some variation between strains in the degree of preference for glycine, in fact 129/Sv and BALB/cAm show no significant preference. In previous work with sweet substances (Lush, 1989) it was found that there is a very high correlation between strains in their degree of preference for four other sweet substances; sucrose, dulcin, acesulfame and saccharin. This was interpreted to mean that the strain variation affects a sweetness receptor which detects all four sweet substances. It was therefore of interest to see if the sweetness of glycine is genetically determined in the same way. When the glycine data in Table 1 are plotted against the results obtained with saccharin from the same strains (data from Lush, 1989) the results shown in Fig. 3 are obtained. There is a correlation ($r_s = 0.67$; $P < 0.01$) between the two sets of data, and this seems to indicate a common genetic causation. However, the correlation is not as high as those previously obtained when comparing the other sweet tastants (Lush, 1989).

To clarify this further, a cross was made between the two strains at the extremes of the glycine range, C57BL/6Ty (93%) and BALB/cAm (40%). Four F₁ mice had a mean result of 80% when tested with glycine, and they were therefore backcrossed to BALB/cAm. The backcross produced 32 progeny and these were tested with glycine and with acesulfame. The latter was chosen in preference to saccharin because it was previously found to be more effective than saccharin in demonstrating the segregation of the *Sac* gene (Lush, 1989). The data obtained with the

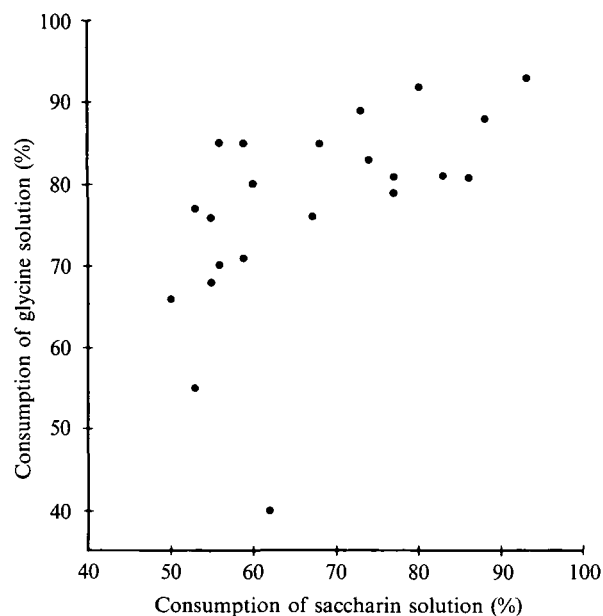


Fig. 3. Consumption of saccharin (1.6 mM) and glycine (200 mM) by 22 strains of mice. Data from Table 1.

32 backcross progeny are plotted in Fig. 4. Every mouse was tested twice with each tastant. With neither of the tastants is it possible to say that there is evidence of segregation of a single gene. But there is clearly a close correlation between the results with the two tastants ($r_s = 0.84$; $P < 0.01$) which supports the hypothesis that the gene or genes which determine the ability to taste acesulfame also have a major effect on the ability to taste glycine.

(iii) Linkage of *Sac*

Strain C57BL/6 mice are tasters when tested with the synthetic sweetener acesulfame. DBA/2 mice are non-tasters. The tasting allele, *Sac*^b, is dominant. The backcross used by Lush (1989) to show segregation of *Sac* was (C57BL/6 × DBA/2) × DBA/2, and its reciprocal (female is written first). Tissues from 27 of the progeny of this original backcross had been stored at -70°C and were available as sources of DNA. In order to increase the numbers for the linkage test, a further 35 progeny were produced from a cross DBA/2 × (C57BL/6 × DBA/2). These were also classified as tasters or non-tasters with acesulfame. Of the total 62 progeny, 31 were tasters and 31 were non-tasters. The marker genes on chromosome 4 which were also segregating in this cross were *Lck* (59 cM from the centromere); *Nppa* (76 cM from the centromere) and *D4Smh6b* (80 cM from the centromere). The map positions are taken from Abbott *et al.* (1993).

Seven progeny were recombinants between *Lck* and *Nppa*. Five progeny were recombinants between *Nppa* and *Sac*. There were no double recombinants. The gene order and the genetic distances are therefore: centromere ... *Lck* - 11.3 ± 4.0 - *Nppa* - 8.1 ± 3.4 -

Sac Sac. Eighteen of the progeny came from F₁ mothers and 44 from F₁ fathers. The *Nppa* - *Sac* distance was 5.5 cM in the former and 9.1 cM in the latter. The difference is not significant. The five recombinants between *Nppa* and *Sac* were typed for *D4Smh6b*. Four of these animals had recombined between *Nppa* and *D4Smh6b* and one between *D4Smh6b* and *Sac*, thus confirming the gene order *Nppa* - *D4Smh6b* - *Sac*. We could not type *Tel4q* in our cross and it remains probable that *Tel4q* is distal to *Sac*, as shown in the map of Abbott *et al.* (1993).

(iv) Linkage of *Soa*

The two genes chosen to test for linkage with *Soa* were *Cd* and *Prp*. These two genes are located 56 cM and 58 cM from the centromere on chromosome 6, respectively (Lyon & Kirby, 1994). Schneider mice have the *Soa*^a allele which confers the ability to taste SOA and is dominant; A/J and the Cd strain have the non-taster allele.

A cross was made between a Schneider female and a Cd/+ male. Two F₁ females with crooked tails were then crossed with strain A/J males. All of their 67 progeny were tested for *Soa* and *Prp* and none showed recombination, so clearly these two genes are very closely linked. The classification of the progeny with respect to SOA tasting and tail phenotype is shown in Table 3. The ratio of 41 tasters to 26 non-tasters does not differ significantly from the expected 1:1 ratio ($\chi^2 = 3.36$, $P > 0.05$). The ratio of 54 normal tail to 13 crooked tail does differ significantly from 1:1 ($\chi^2 = 25.1$, $P < 0.005$) but this can be explained in terms of the incomplete penetrance of the *Cd* allele.

Bailey (1950) derived two formulae which are useful in this situation. Formula (i) below gives a maximum likelihood estimate of λ which is the proportion of Cd/+ mice which have normal tails, in other words the degree of non-penetrance of *Cd*. Using letters to represent the four classes of progeny as shown in Table 3, this formula is:

$$\lambda = \frac{(cd - ab)}{(a + c)(b + d)} \quad (\text{i})$$

and the value of λ from our data is 51.4%. Formula (ii) gives a maximum likelihood estimate of the recombination fraction p

$$p = \frac{b(a + c)}{b(a + c) + a(b + d)} \quad (\text{ii})$$

and with our data $P = 0.05$, that is a genetic distance between *Cd* and *Soa* of 5.0 cM.

4. Discussion

The data from the strain survey (Fig. 1) and from the backcross (Fig. 2) show that the gene *Glb* determines the ability to taste the bitterness of copper glycinate. This probably extends to the copper salts of a number of other amino acids. It seems unnecessary to change

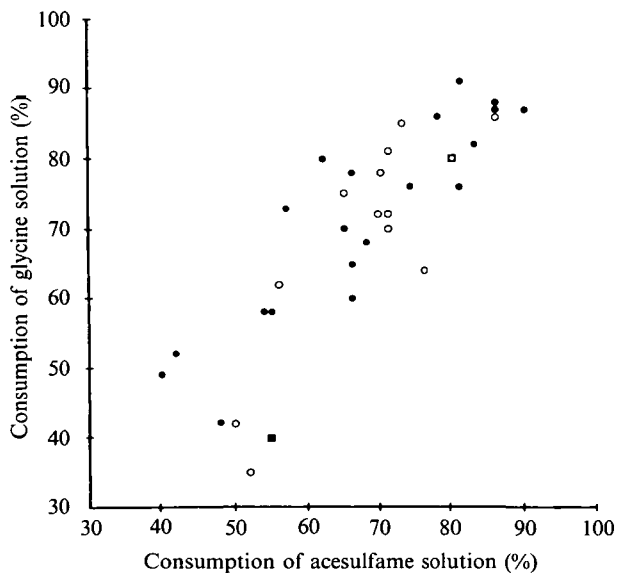


Fig. 4. Consumption of acesulfame (5 mM) and glycine (200 mM) by 32 progeny of the backcross BALB/cAm \times F₁ (C57BL/6Ty \times BALB/cAm). \square , mean of 4 F₁ mice. \bullet , BALB/cAm. The empty circles represent 12 non-albino progeny which were homozygous for the brown coat colour gene *b*.

the gene symbol *Glb*, which can now refer to *glycinate* bitterness rather than *glycine* bitterness. The close linkage of *Glb* and *Rua* has been confirmed.

In a previous paper (Lush, 1989) it was shown that most of the difference between C57BL/6 and DBA/2 in their ability to taste sweet substances can be attributed to one gene, *Sac*. It is not known whether *Sac* acts on the peripheral sweetness receptor or on some more central site within the brain, but for the sake of brevity we shall assume that it acts on the sweetness receptor. The progeny of the backcross shown in Fig. 4 do not fall into two groups, and so it seems that there must be more than one gene determining the difference between C57BL/6 and BALB/cAm. This need not alter the conclusion that there is only one sweetness receptor in the mouse; it simply means that the structure or function of the sweetness receptor can be affected by more than one gene. A candidate for this role is the gene *dpa* described by Ninomiya *et al.* (1991). This gene determines the response of mice to a 0.1 M solution of D-phenylalanine, which is moderately sweet to

humans. C57BL/6 mice are tasters and C3H and BALB/c mice are non-tasters. The technique used to classify individual mice involved the intraperitoneal injection of a toxic chemical (LiCl) so as to set up a conditioned aversion to the taste of D-phenylalanine. Ninomiya *et al.* (1991) mapped *dpa* to chromosome 4 at about 14.4 cM proximal to *b* (brown coat colour). The gene *dpa* must be different from *Sac* because we have mapped the latter to the other end of chromosome 4, about 8.1 cM distal to *Nppa*. The *b* allele is present in the BALB/c strain and the backcross progeny shown in Fig. 4 were therefore segregating for *b*. Eleven of the progeny were albino, and 12 of the 21 pigmented mice were homozygous *bb*. If the gene *dpa* is involved in the variation seen on these progeny with respect to glycine and acesulfame one would expect the homozygous *bb* mice to be found mainly near the lower end of the distribution because of the close linkage between *dpa* and *b*. But in fact the *bb* mice were uniformly distributed, as can be seen in Fig. 4 where the *bb* mice are symbolized by open circles. This seems to indicate that there are two independently-acting sweetness genes; *Sac* which determines a receptor with wide specificity, and *dpa* which determines a D-phenylalanine receptor. Clearly more work is needed to sort out the relationship between *Sac* and *dpa*. Ninomiya *et al.* (1991) are confident that *dpa* is expressed peripherally at the level of the cell membrane or receptor. But the fact that their mice were not allowed to choose spontaneously but were experimentally conditioned to reject D-phenylalanine raises the possibility that the difference between their tasters and non-tasters is to some extent due to differences in response (pharmacological or neurological) to the toxic injection of lithium chloride rather than differences in perception of the taste of D-phenylalanine.

Prp and the four bitterness-tasting genes *Cyx*, *Qui*, *Rua* and *Glb* are known to be closely clustered because they have almost identical SDPs in the BXD and CXB RI strains. The linear order of the tasting genes is probably as given above, but the genetic distances between them are not accurately known (Lush & Holland, 1988). The estimate of 5 cM between *Cd* and *Soa* is consistent with *Soa* being very close to *Prp*.

No recombination between *Prp* and *Rua* has been detected in RI or congenic strains, and our present

Table 3. Phenotypic classification of 67 backcross progeny demonstrating linkage between *Cd* and *Soa*

	Parental		Recombinant	
	Taster	Non-taster	Non-taster	Taster
Tasting phenotype:	Normal	Crooked	Normal	Crooked
Tail phenotype:	Normal	Crooked	Normal	Crooked
No. of progeny:	40	12	14	1
Symbols used in formulae (i) and (ii):	d	a	c	b

data show no recombination between *Prp* and *Soa*. Therefore, these three genes, *Soa*, *Rua* and *Prp* all map to the same position on chromosome 6 at about 58 cM from the centromere. In view of the fact that SOA and RUA (raffinose undecaacetate) are both acetylated sugars it has been suggested that *Soa* and *Rua* are not separate genes but are merely different alleles of the same gene (Harder *et al.* 1992).

It seems reasonable to suppose that the individual bitterness-tasting genes which make up the cluster on chromosome 6 have evolved from one original bitterness gene by a process of local duplication and differentiation. It is tempting to extend this idea and speculate that the original bitterness gene and the sweetness gene, *Sac*, also had a common origin. We do not have any sequence data for any of the tasting genes, or their products, so the evidence is at present circumstantial.

It has been argued by Ohno (1970) that the increase in genome size which accompanied the evolution of higher vertebrates from their fish-like ancestors was largely caused by polyploidy. An early tetraploidization event doubled the DNA in the genome, and this was followed by a slow mutational divergence of chromosomes which had originally been homologues. This process of divergence is referred to by Ohno (1970) as diploidization. At the start of the process each gene was present four times in the tetraploid genome, and this redundancy allowed one of each pair of loci either to take on a new function or to become non-functional ('silent') during diploidization. Within a species, two loci which have diverged in this way from a common ancestor are said to be paralogous.

These ideas have been persuasively applied by Lundin (1979, 1993; see Nadeau *et al.* 1992) who compared gene arrangements in different chromosomes in mouse and man and suggested several examples of paralogies within each species and homologies between the species. In the present case we propose that part of mouse chromosome 4 and part of chromosome 6 have a number of paralogous loci, including the tasting loci. This implies that these two chromosome segments have evolved from a common ancestor chromosome in the manner described above. The number of loci which can be adduced to support this hypothesis has been noted elsewhere (Lush, Hornigold & Stoye, 1993) and the argument will be presented in detail in a later paper.

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