

target cells for the vitamin. If the uptake of vitamin D in bone is to be measured by quantitative determination of extracts from homogenates, the relatively high uptake in bone marrow and surrounding connective tissue might be interpreted erroneously as an accumulation in bone. The accumulation of radioactivity in connective tissue may be of significance with regard to the reported stimulatory effect of vitamin D on bone collagen synthesis<sup>9</sup>.

There was only moderate accumulation of radioactivity in the intestinal mucosa during the whole observation period. Because of the high intestinal radioactivity content, and because of a probable absorption of radioactivity from the lumen, the significance of these results is difficult to interpret.

An interesting finding was the relatively high accumulation of radioactivity in certain endocrine organs such as the thyroid, hypophysis, and adrenal cortex. As can be seen in Figure 3, the uptake in the thyroid is highest at certain localities, which do not entirely coincide with follicles, and it is thus possible that the activity represents

an accumulation in the calcitonin-producing parafollicular cells. The activity in the parathyroid, however, is low (Figure 3). Calcitonin has been shown to enhance the production of 1,25-DHCC in the kidneys of rats<sup>10</sup>. Vitamin D causes a degranulation of the parafollicular cells in cows also in the absence of significant hypercalcaemia<sup>11</sup>. A direct effect of vitamin D on the parafollicular cells might be considered as a possible link in the complicated regulation of the calcium-homeostasis.

In the fetus, the concentration of radioactivity was very low 24 h after injection. However, after 4 days the concentration was as high as in the mother, and the distribution pattern was also similar to that seen in the mother at this long time after injection. Thus, there was a localized uptake of radioactivity in certain areas of the kidney. The uptakes in thyroid, adrenal cortex and hypophysis seemed to be relatively a little higher than in the mother. The delayed uptake in the fetus may indicate that a metabolite, and not vitamin D<sub>3</sub> itself, is transferred to the fetus. The accumulation in the fetal kidney may also suggest that the fetus has the ability to convert 25-HCC to 1,25-DHCC. It has been claimed that the fetus cannot metabolize vitamin D<sub>3</sub> and that 25-HCC rather than vitamin D<sub>3</sub> passes to the fetus<sup>12</sup>. There was also an accumulation of radioactivity in the yolk sac epithelium, as has been found for a number of other substances<sup>13</sup>. Its importance is, however, not well understood.

*Zusammenfassung.* Mit Hilfe der Ganzkörper-Autoradiographietechnik konnte nach Zufuhr von Vitamin D<sub>3</sub>-4-<sup>14</sup>C an Mäusen der Nachweis einer radioaktiven Ansammlung in gewissen Gebieten (Labyrinth) der Nierenrinde sowie der Thyroidea erbracht werden, die möglicherweise mit parafollikulären Zellen identisch ist.

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Semiquantitative evaluation of whole-body autoradiograms after s.c. injection of vitamin D<sub>3</sub>-4-<sup>14</sup>C

	Time (h)			
	1	8	24	96
Kidney (parts of cortex)	16	128	1024	1024
Liver	128	256	256	128
Mucosa of small intestine	128	128	128	128
Thyroid	8	128	128	64
Hypophysis	8	128	128	64
Adrenal cortex	8	128	128	64
Brown fat	8	128	128	128
Bone marrow	4	128	128	32
Connective tissue	4	16	128	128
Blood	4	16	64	32
Intestinal contents	512	512	1024	512

The radioactivity in different organs was compared with autoradiograms of simultaneously exposed <sup>14</sup>C-isotope-staircases<sup>8</sup>. These consisted of 10 steps of increasing isotope concentration in the geometric series 2<sup>1</sup> (2), 2<sup>2</sup> (4), 2<sup>3</sup> (8) ... 2<sup>10</sup> (1024). The radioactivity for the different localities is expressed as the relative isotope concentration of the staircase step with which it matched. The radioactivity in bone never exceeded the lowest step of the staircase, and has therefore not been included in the table.

<sup>9</sup> F. CANAS, J. S. BRAND, W. F. NEUMAN and A. R. TEREPA, *Am. J. Physiol.* 216, 1092 (1969).

<sup>10</sup> L. GALANTE, K. W. COLSTON, S. J. MACAULEY and I. MACINTYRE, *Nature, Lond.* 238, 271 (1972).

<sup>11</sup> D. M. YOUNG and C. C. CAPEN, *Virchows Arch. path. Anat. Physiol.* 8, 288 (1971).

<sup>12</sup> H. RIKKERS, *Pediatr. Res.* 4, 442 (1970).

<sup>13</sup> L. DENCKER and S. ULLBERG, in preparation.

## Asymmetrical Responses to Directional Selection for Radiation Resistance and Sensitivity in *Drosophila*

Genetic variation for resistance and sensitivity to extremely high doses of <sup>60</sup>Co γ-radiation has been reported in *D. melanogaster*<sup>1-3</sup>; as assessed by scoring percentage mortality after short periods of time. In this article we report on an attempt at exploiting such genetic variation by carrying out directional selection. Since the high doses of radiation used lead to immediate sterilization and early death, it was necessary to employ a method of sib-selection<sup>4</sup> where selection is based only on the values of relatives. A response to selection in such circumstances implies that the hereditary variability must already be present in the population, as the selected flies are never themselves exposed to the selective agent.

The experiments were started from strains set up from single inseminated females collected from a population polymorphic for radioresistance at Leslie Manor (LM) near Camperdown, Victoria in 1965<sup>2</sup>. Initially, 3 resistant LM strains were crossed together and 3 sensitive LM strains

<sup>1</sup> M. OGAKI and E. NAKASHIMA-TANAKA, *Mutation Res.* 3, 438 (1966).

<sup>2</sup> P. A. PARSONS, I. T. MACBEAN and B. T. O. LEE, *Genetics* 61, 211 (1969).

<sup>3</sup> J. M. WESTERMAN and P. A. PARSONS, *Int. J. Radiat. Biol.* 21, 145 (1972).

<sup>4</sup> D. S. FALCONER, *Introduction to Quantitative Genetics* (Oliver and Boyd, Edinburgh and London 1960).

Table I. Percentage mortalities\* and realised heritabilities of flies 1 day after irradiation

Selection line	Percentage mortalities						Realised heritabilities
	Generation 0	1	2	3	4	5	
RS-1	25.6	34.0	4.0	13.7	65.6	62.1	$-0.26 \pm 0.17$
RS-2	25.6	6.5	2.8	3.5	21.9	76.4	$-0.32 \pm 0.24$
RR-1	25.6	14.1	3.3	1.1	3.7	0.1	$+0.79 \pm 0.24$
RR-2	25.6	7.0	5.5	5.5	4.1	0	$+0.48 \pm 0.17$
SS-1	60.4	88.4	53.5	84.3	80.2	61.0	$+0.01 \pm 0.19$
SS-2	60.4	55.1	17.8	40.8	64.7	29.0	$+0.12 \pm 0.31$
SR-1	60.4	53.4	28.4	15.2	18.2	18.0	$+0.49 \pm 0.01$
SR-2	60.4	84.3	24.9	4.9	8.6	3.0	$+0.97 \pm 0.29$

\*Each entry in the table is the mean of 2 replicates of 25 female flies.

were crossed together to provide large pools of variability for resistance and sensitivity. From both the Resistant (R) and Sensitive (S) populations, 24 single pair matings were set up, and for each mating 2 replicates of 25 virgin females, aged 4 to 6 days, were exposed to 110,000 rads of  $^{60}\text{Co}$ - $\gamma$ -radiation. Females only were irradiated as the results obtained are more reproducible than those based on males. Irradiations were carried out at the Australian Atomic Energy Commission Research Establishment, Lucas Heights, N.S.W.

Table II. Percentage mortalities\* of the lines after selection and the 6 LM strains 1 day after irradiation

Line	Females	Males
RS-1	67.9	98.8
RS-2	50.8	99.0
RR-1	3.2	65.9
RR-2	2.0	15.8
SS-1	100	100
SS-2	85.8	98.9
SR-1	22.8	82.0
SR-2	9.6	76.1
LM-R 1	30.4	82.0
2	12.5	62.7
3	0	7.5
mean	14.3	50.7
LM-S 1	38.8	83.3
2	87.8	92.4
3	60.9	96.0
mean	62.5	90.6

\* Each entry is the mean of 2 replicates of 25 flies.

Table III. Analysis of variance, after angular transformation, of the selection lines in Table II

Source	d.f.	M.S.
Lines	7	2551.05*
Sexes	1	6845.08*
Lines $\times$ sexes	7	300.23
Interactions	16	125.39

\*  $P < 0.001$

Two replicate R and S lines were selected from both the R and S populations, giving 8 selection lines altogether. These 8 lines were maintained by setting up 6 single pair matings each generation, irradiating 2 female replicates, and selecting in the required direction. Unfortunately, selection had to be terminated after only 5 generations, even so, the results are of sufficient interest to report here. The 4 possible types of selection lines are written as RR, SR, SS and RS where the first letter refers to the population on which selection was based (R or S), and the second to the type of selection carried out.

Percentage mortalities were scored 1 day after irradiation, and the results are shown in Table I. Even in the short time available, striking responses to selection for all 4 R lines (RR-1, RR-2, SR-1, SR-2) were obtained. In contrast, the 2 replicate SS lines did not respond to selection, but fluctuated widely. Percentage mortalities of the RS lines fell initially, but then rose steeply in the direction of selection. Further generations of selection would be required to test if this is a true response.

After applying the angular transformation, realised heritabilities were calculated by regressing these responses onto the cumulative selection differentials. The realised heritabilities given in Table I are all positive and significant for the R lines as expected, but in no case are significant values obtained for the S lines, and in fact 2 of the values are negative.

After the 5 generations of selection, each of the 8 selection lines was mass-mated and compared with the 6 LM strains forming the original R and S base populations. 2 replicates of 25 virgin females and males separately were irradiated with 110,000 rads. Mean percentage mortalities are shown in Table II, and the analysis of variance of the selection lines after angular transformation in Table III. As expected, there are differences between lines and between sexes, males being more sensitive than females as is usual. There is, however, no significant interaction between lines and sexes, indicating that the difference between males and females in different lines is proportional.

We may conclude, therefore, that selection has been very effective for resistance but not so far for sensitivity. Radioresistance can be argued to be a trait subject to stabilizing selection<sup>2</sup> (which implies an intermediate optimum), but it does show some dominance over sensitivity in diallel cross data<sup>2</sup> so that an asymmetrical response to selection in the direction of radioresistance may be reasonable. For more conventionally studied traits under stabilizing selection e.g. litter size, body weight and lactation in mice, and other traits in several

organisms<sup>4-6</sup>, asymmetrical responses to directional selection are common.

Although stress traits have rarely been selected for both resistance and sensitivity in one experiment, there are reports of quite rapid responses to selection for resistance to specific stresses such as DDT in *D. melanogaster* and other species, presumably due to the rapid rearrangement of additive genes<sup>7,8</sup>. Like radioresistance, dominance has been found for resistance to various insecticides and anaesthetics such as ether<sup>8,9</sup>. Therefore in conclusion, asymmetrical responses to selection for stresses may be reasonable, such that resistant strains are rapidly built up as is known for DDT. The other important conclusion is that it has been possible to show through sib-selection that the genetic variation for radioresistance present in the base populations can be selected without any contact with the selective agent<sup>10</sup>.

**Zusammenfassung.** Es wurde eine Selektion auf Strahlenresistenz nach Bestrahlung von *Drosophila melanogaster* mit <sup>60</sup>Co- $\gamma$ -Strahlen während 5 Generationen mit gutem Erfolg erzielt, nicht aber eine solche auf

erhöhte Strahlensensibilität. Der asymmetrische Selektionseffekt dürfte somit auf dominanter Vererbung der Resistenz beruhen. Familienselektion kann auch ohne Bestrahlung zu resistenten Stämmen führen.

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### Cordycepin Inhibits Induction of Puffs by Ions in *Chironomus* Salivary Gland Chromosomes

Puffs in polytene chromosomes of Diptera are inducible by inorganic<sup>1</sup> and organic ions<sup>2</sup>. Both types of ion act directly at the chromosomal level<sup>3,4</sup> and may be implicated in the control of gene activity by hormones during normal development<sup>5</sup>. Incubated in the absence of RNA precursors, isolated polytene chromosomes react to changes in their electrolyte milieu by a differential decondensation of bands at specific loci<sup>3,4</sup>. From this it could be concluded that induction of puffs by ions is exempt from the general rule that puffs can persist or be induced only under conditions permitting RNA synthesis. This would mean that puff induction by ions exhibits biochemical characteristics different from those observed during induction of puffs by ecdysone<sup>6</sup>. However, in this com-

munication I present evidence that in intact cells an unimpaired capacity for RNA synthesis is required for the induction of puffs by inorganic and organic ions.

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<sup>6</sup> M. ASHBURNER, Expl Cell Res. 71, 433 (1972).

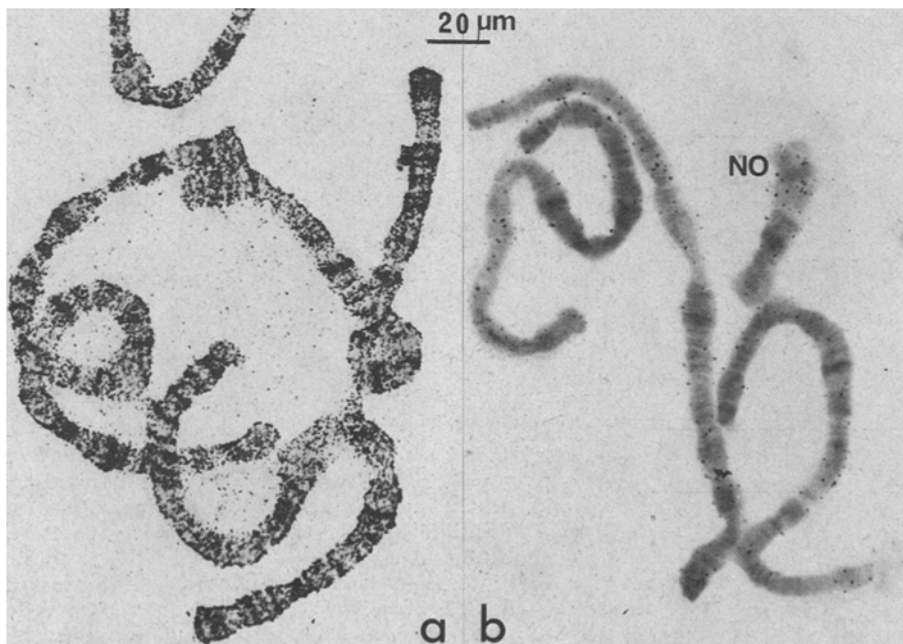


Fig. 1. Effect of cordycepin on <sup>3</sup>H-uridine incorporation into salivary gland nuclei of *Chironomus thummi*. a) control in TM I and b) sister gland in TM I with 100 µg/ml cordycepin. NO = nucleolus organizer.