Table 1. Results of experimental transformation of *Haideotriton wallacei*: ++, complete transformation; +, partial transformation; −, no change.

Concentration of thyroxin (μg/lit.)	Time treated (days)	Body length (mm)	Sex or stage	Loss of fins	Loss of labial folds	Gill atrophy	Narial shift to adult position	Development of gular fold	Loss of lateral line organs	Atrophy of coronoid
10,000	15	27	F	+	++	+	+	−	+	++
2,000	18	22	F	++	++	+	+	+	++	++
2,000	25	25.5	F	+	++	+	+	+	++	++
500	17	16	Immature	++	++	+	++	++	++	+
500	18	18	Immature	++	++	+	+	+	++	++

opment of adult vomerine tooth pattern and of choanal notches in the vomers; ossification of parasphenoid bone; and development of parasphenoid dentition.

Haideotriton, though exhibiting limited response to thyroxin, possesses distinct thyroid follicles containing colloid. A histological preparation made from the throat region of an untreated female approximately 24 mm from snout to vent contains a series of small follicles on either side, spread over an anteroposterior distance of 520 μ. The follicles, which do not exceed 30 μ in diameter, are lined with squamous-to-low-cuboidal epithelium. No attempt was made to identify thyroid hormone in the colloid, but as the experiment shows, the mere existence of an ample supply of thyroxin does not insure that metamorphosis will occur. Thus, *Haideotriton,* like *Necturus* and *Typhlomolge,* appears to be genetically resistant to the thyroid secretions, even though the animals' own thyroids produce and presumably release thyroid hormone or hormones.

Haideotriton proves to be the most resistant to thyroxin of all the plethodontids investigated. The results of the experiment described indicate that *Haideotriton* should be recognized as a plethodontid that has deviated markedly from other members of its family in that it has lost many of the usual adult bony structures and integumentary features, probably through genetic change. In many cases a classification of family is based upon the lack of certain bones found in more generalized families, but we see here a case where relationships are based only on larval similarities.

A moot point, then, is where to draw the line in declaring a higher category, for in a sense *Haideotriton,* and for that matter *Typhlomolge,* each of which lacks certain bones, is not comparable to transformed plethodontids and could represent independently lungless salamanders of a closely related but different family. If *Haideotriton* and *Typhlomolge* are retained as plethodontids we must realize that the characteristics of animals in which neoteny occurs should be defined on the basis of both larval and adult features, so that the full identity is known. Thus, the characteristics of a salamander family are not solely those given for the transformed adult, and the necessity for concise descriptions of larvae is strongly indicated (*5*).

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New Genetically Homogeneous Background for Dystrophic Mice and Their Normal Counterparts

Abstract. A new type of genetically homogeneous dystrophic and comparable normal mice, from an F_1 hybrid cross between 129/Re-*dy* and C57BL/6J-*dy,* is now available as a result of a special breeding program. The clinical manifestations in these F_1 hybrid dystrophics correspond closely with those observed in 129/Re-*dydy* mice, and they give completely comparable results on a variety of research tests. They are, however, considerably healthier than previously available dystrophics, with a growth rate closer to normal and a greatly increased life-span.

A research development at the Roscoe B. Jackson Memorial Laboratory which may be of interest to investigators studying muscular dystrophy in other institutions is the recent production of genetically uniform F_1 hybrid dystrophics (*dydy*) and comparable normal (*DyDy* and *Dydy*) counterparts. These animals come from a cross between the 129/Re-*dy* and C57BL/6J-*dy* inbred strains, made possible by the introduction of the *dy* gene onto the C57BL/6J background by repeated backcrossing, now at backcross 10. At this backcrossing generation, approximately 98 percent of genes not closely linked to *dy* are expected to be identical with those of C57BL/6J (*1*).

As in the case of regular maintenance of *dy* in its strain of origin, 129/Re (*2*), this breeding program has involved transplantation of *dydy* ovaries into histocompatible normal host females (*3*). In each successive backcross generation, host females were F_1 hybrids between inbred strains 129/J and C57BL/6-$a^t a^t$. These females accept tissues from all backcross generations, since they carry one dose of all histocompatibility alleles carried by both of the original parental strains (*4*), and have the added advantage of providing genetic markers (A^w, a^t) for identification of possible offspring from regenerated host ovaries. These host females, bearing ovaries transplanted from black dystrophic (*aa B- C- dydy*) females (offspring of *Dydy* carriers from the previous backcross generation), were mated to C57BL/6J (*aa BB CC DyDy*) males. The resulting *Dydy* offspring were intercrossed, and their dystrophic female offspring used in the next backcross generation.

There is little to choose in health or survival time between dystrophic individuals in the two inbred strains, 129/Re-*dy* and C57BL/6J-*dy*. When a cross is made between carrier individuals from these two inbred strains, clearly identifiable *dydy* individuals, showing the characteristic dystrophic syndrome (*5*) appear in the expected proportion. These are, however, considerably healthier, show less difference from normal in weight, and survive much longer than the dystrophics in either parental strain. Although 17 littermate comparisons (Table 1) of the body weight of *dydy* dystrophics and normals confirmed previous observations (in 129/Re) of significant size difference between genotypes, the weight differential was less than is usually observed in 129/Re-*dy* and all individuals appeared to thrive.

The contrast in life-span of inbred and uniform F_1 hybrid dystrophic animals is very striking. The mean life-span of 129/Re-*dy* dystrophics on a good laboratory diet is approximately 180 days (*6*), that of C57BL/6-*dy* dystrophics 106 days (*7*). It is not yet possible to estimate the *mean* life-span of 129B6-*dy* F_1 dystrophics, but 47/50

Table 1. Comparison of mean body weights (in grams) up to weaning of 129B6-*dy* uniform F_1 hybrid dystrophics, their normal littermates, with 129/Re-*dy* dystrophics and normals.

Age (day)	Genetic background	*dydy* ♀		*Dy-* ♀		*dydy* ♂		*Dy-* ♂	
		No.	Mean wt.	No.	Mean wt.	No.	Mean wt.	No.	Mean wt.
14	129B6 F_1	6	7.3	6	8.4	3	8.3	3	10.3
21	129B6 F_1	5	10.6	4	13.0	6	10.6	5	13.1
28	129B6 F_1	6	15.0	6	17.3	11	15.8	10	19.3
28	129/Re	12	12.4	12	17.6	5	12.6	7	19.4

(94 percent) set aside for longevity studies have survived more than 150 days, and 43/50 (84 percent) have survived 210 days. Their *median* life-span is close to 250 days.

The increased vigor and prolonged life-span of uniform 129B6-*dy* F_1 dystrophics suggests that they may be much more useful animals for many research projects than are the presently used 129/Re-*dy* dystrophics. It should be stressed that although 129/Re-*dy* × C57BL/6J-*dy* F_1 hybrid dystrophics are heterozygous for all genes by which 129/Re and C57BL/6J differ, it is still true that all individuals *within* one F_1 hybrid group are as much like each other as are the members of a single inbred strain. It is also true that 129B6 F_1-*DyDy* and 129B6 F_1-*Dydy* differ from the 129B6 F_1-*dydy* largely only by these allelic genes at the dystrophy locus, making them good normal and carrier controls. (A word of caution might be inserted regarding the high degree of genetic heterogeneity in offspring of 129B6 F_1 carriers; such progeny are not desirable for experimental use.)

Uniform 129B6 F_1-*dy* dystrophics exhibit clear-cut expression of the dystrophy syndrome at 2 to 3 weeks, and show progression of the disease during their extensive life-span. We anticipate they will withstand shipping better than do 129/Re-*dydy* mice. Small numbers of 129B6 F_1-*dy* dystrophics have been used at the Roscoe B. Jackson Memorial Laboratory for histological studies at 2 and 6 weeks postnatal (*8*), determinations of glycine transamidinase activity (*9*), measurements of acetoacetate accumulation (*10*), and experiments in artificial insemination (*11*). In these investigations results were obtained completely comparable with those in which 129/Re-*dydy* dystrophics were used. For many experiments, these 129B6 F_1 hybrid animals should give results identical with those obtained with 129/Re-*dydy* dystrophics. For other experiments, it may be necessary to establish new base lines fitting with the new background genetics. For some investigators the improvement in health and viability may not be worth this effort. However, we would like to suggest that these 129B6 F_1-*dy* dystrophics and their normal counterparts may become the animals of choice for many types of research (*12*).

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Inactivity in vivo of Transcortin-Bound Cortisol

Abstract. By means of a liver glycogen maintenance assay for corticosteroids, it was shown that transcortin-bound cortisol is biologically inactive.

From indirect evidence we previously postulated that transcortin-bound cortisol appears to be biologically inactive (*1*). Now we report experimental verification of this hypothesis, based on the observation that mice treated with transcortin were unable to respond to cortisol in a standard glycogen maintenance assay (*2*).

Transcortin was isolated from the plasma of patients with carcinoma of the prostate, who had been on diethylstilbesterol therapy (15 mg/day) for over 3 months. This type of plasma was chosen because of its high concentration of transcortin (*3*). Similar concentrations prevail during the third trimester of pregnancy (*1*). Although there is a possibility that the transcortin in the plasma of the cancer patients may differ from that in the plasma of normal or pregnant subjects, data obtained to date indicate that there is no difference in the physiological action of these transcortins (*1, 3, 4*). Furthermore, the chemical and physical properties of transcortin isolated from normal plasma are similar to those of the transcortin isolated from the serum of estrogen-treated patients with cancer of the prostate (*5*). The method of isolation, details of which will be published elsewhere, consisted of a gradient from 0.05*M* to 0.075*M* sodium chloride at a constant *p*H of 5.0 on a column of diethylaminoethylcellulose. The material eluted just prior to caeruloplasmin was used for injection.

Cortisol was assayed in adrenalectomized male Swiss mice according to published directions (*2*), with the exception that instead of adrenal cortical extract the animals received subcutaneously 100 μg of cortisol in 0.25 ml of corn oil after adrenalectomy and 200 μg of cortisol in 0.4 ml of corn oil 16 hours before commencement of the assay. At zero time each mouse received intravenously an amount of transcortin, which was calculated from binding data for each batch of transcortin to bind a minimum of 80 to 90 percent of the administered cortisol. Each animal then received 10 or 15 μg of cortisol subcutaneously in seven divided doses at hourly intervals. In one control group the transcortin was omitted, in the other the cortisol. Liver glycogen was assayed by the anthrone method (*6*), care being taken to add the anthrone reagent to the tubes while they were immersed in an ice bath. After the tubes had been heated for 10 minutes in boiling water, they were returned to the ice bath. This modification gave greater uniformity. The optical density of the greenish solutions was read in a Beckman model B spectrophotometer at 630 mμ.

From the results given in Table 1 it is evident that transcortin by itself has no demonstrable effect on the levels of liver glycogen. On the other hand, 10 to 15 μg of cortisol produce a definite response. The levels of 6.2 and 7.1 mg of glycogen per 10 g body