zygous and the other half heterozygous, I am attempting to breed these males in order to determine whether there is a correlation between genotype and phenotype. The female siblings exhibit a considerable range of variation in the expression of the P^2 allele but the variation is continuous. These fish are being bred as well.

There is reason to suspect that such a correlation may exist in males. The 2185 pedigree contained both heterozygous and homozygous males and although none of these males exhibited atypical pigmentation, as a group they showed a bimodal distribution of degree of pattern expression. I classified the males of 1 brood according to the degree of pattern expression and predicted that those individuals with poor expression would prove to be heterozygous and those with good expression, homozygous. Seven of these fish were successfully bred (Table II) and 5 of the predictions proved true, 1 proved false and in the 7th case the fish was considered to have been intermediate so no firm prediction had been made[7].

Population hybrids in this species may also exhibit enhancement of the P^2 pattern. The 2122 pedigree was derived from a female collected in Arroyo La Flor and a male collected in Arroyo Sarco. These two localities within the Rio Sabinas system are 8 km apart as the fish swims. Two 2122 males developed melanomas and 1 exhibited atypical pattern enhancement by the age of 20 months. Eleven other P^2 males in this pedigree did not show atypical pigmentation but not all of these survived long enough for this to have developed. Figure 3 illustrates one of the melanotic individuals.

I estimated the percentage of surface area covered by the P^2 pattern for adult fish of the 2122 and 2123 pedigrees and found that the pattern was significantly better expressed in males[8]. Although the 3 fish destined to develop atypical pigmentation were included in this analysis, this may indicate that males are more prone to develop melanomas than are females. That is, it may be significant that all 4 examples of atypical pattern enhancement reported here involved males. This is particularly interesting because SICILIANO, PERLMUTTER and CLARK[9] report that in hybrids of *X. maculatus* and *X. helleri* which have inherited the Sd gene of the former species and therefore develop melanomas, males develop the melanomas earlier than do females. KALLMAN[10] points out that the Sp^8 gene in *X. maculatus* produces a prominent black spot in males that does not show up in females. The P^1 pattern of *X. variatus* also has better expression in males than in females[3].

There is only one other reported case of melanomas in non-hybrid *Xiphophorus*; the Sc gene in an inbred strain of *X. montezumae cortezi* causes their production in some of the carriers[11]. The present report indicates that melanomas may be normal, although very rare events in platyfish populations.

It is interesting to speculate on the consequences of melanomas in natural populations of these fish. The P^2 gene appears to be found only rarely on the *Y* chromosome in the Rio Sabinas populations but is found on both the *X* and the *Y* chromosome in the population inhabiting its tributary, the Arroyo Sarco. Since crossing over between the gonosomes occurs in *Xiphophorus*[12], the bias in the main river populations indicates that *Y* chromosomes bearing the P^2 allele are selectively eliminated. The lack of bias in the Arroyo population indicates that the selective agent at work in the river populations is not at work in the Arroyo populations. From the observations I have reported it appears that homozygous males have the highest risk of developing melanomas and such a factor would tend to limit the P^2 allele to the *X* chromosome. The melanomas reported in this paper developed only in older fish and this could account for the difference between the 2 populations. Annual flooding appears to wash adults from the steeply banked Arroyo Sarco[3] so most males would not live long enough for melanomas to develop. In the main river with its broad flood plains, the impact of flooding is decreased and enough males would survive to an age at which the melanoma factor could become important[13].

Zusammenfassung. Nachweis von genetisch bedingten Melanomen bei Wildfängen der reinen Art des Zahnkarpfen *Xiphophorus variatus*, wobei es sich eindeutig nicht um einen Artbastard handelt.

R. BOROWSKY

Department of Biology, New York University, (New York 10003, USA),
26 April 1973.

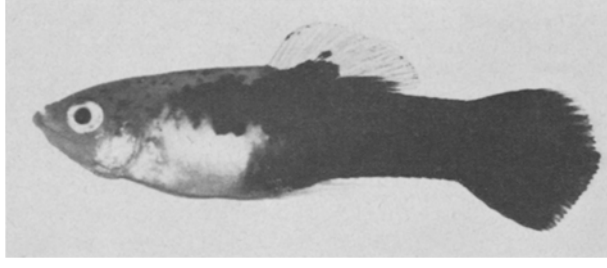

Fig. 3. One of the 2122 males with a melanoma. The nodule was on the side of the fish and is not visible in this photograph but the enhancement of the P^2 patern is clear.

[7] $P = 0.11$.

[8] For the 2122 pedigree: 3 females, range of 4.3–7.3%, median = 7.2%, 10 males, range of 4.2–36.5%, median = 8.8%, $p = 0.143$ (WILCOXON's *t*-test). For the 2123 pedigree: 3 females, range of 1.7–2.4%, median = 1.9%, 4 males, range of 2.5–21.3%, median = 7.25%, $p = 0.029$. The significance of the combined results evaluated by means of the KOLMOGOROV-SMIRNOV statistic: $p = 0.05$.

[9] M. J. SICILIANO, A. PERLMUTTER and E. CLARK, Cancer Res. *31*, 725 (1971).

[10] K. D. KALLMAN, Zoologica *55*, 1 (1970).

[11] K. D. KALLMAN, Zoologica *56*, 77 (1971).

[12] P. A. MACINTYRE, Am. Nat. *95*, 323 (1961).

[13] This work was supported in part by grant No. CA 06665 of the USPHS and in part by a grant from the Arts and Sciences Research Fund of New York University. I thank Dr. K. D. KALLMAN for the provision of facilities and his advice.

Action of Antituberculosis Drugs on Human Leukocyte Chromosomes in vitro

Due to the high incidence and prevalence in the developing countries, tuberculosis invariably represents the most frequently found infectious disease in the world. Therefore millions of patients must continuously undergo long-term treatment with antituberculosis drugs in triple or double combinations. Moreover, many healthy individuals with a high risk of catching tuberculosis are treated with isoniazid (INH) as primary or secondary chemo-

Chromatid aberrations induced by *para*-aminosalicyclic acid (PAS), ethambutol (EMB) and capreomycin (CM) in human lymphocytes in vitro

Substance concentration (mg/ml) treatment time (h)	Number of cells analysed	Achromatic lesions (AL) % of cells	Achromatic No. per cell	Chromatid breaks (B′) % of cells	Chromatid No. per cell	Isochromatid breaks (B″) % of cells	Isochromatid No. per cell	Sum total of all breaking events per cell cell[c]
PAS, 0.153								
48	200[a]	10.00	0.125	3.50	0.035	2.00	0.020	0.075
24	200[a]	10.00	0.110	5.00	0.050	2.50	0.030	0.110
6.5	200[b]	9.00	0.115	6.50	0.070	2.00	0.020	0.110
EMB, 0.028								
48	200[a]	6.50	0.070	3.50	0.035	2.00	0.020	0.075
24	200[b]	7.50	0.080	4.00	0.040	2.50	0.025	0.090
6.5	150[b]	13.33	0.173	6.00	0.060	0.60	0.006	0.073
CM, 0.015								
48	100[a]	11.00	0.110	3.00	0.030	–	–	0.030
24	200[b]	5.00	0.060	4.00	0.040	1.50	0.020	0.080
6.5	200[b]	5.00	0.060	3.00	0.030	1.00	0.010	0.050

[a] 3 cultures. [b] 2 cultures. [c] Calculated from B′ = 1 and B″ = 2.

prophylaxis. The widespread application of antituberculosis drugs makes it very important to test their possible genetic hazards.

Microcultures (slightly modified from ref. [1]) were set up with the blood of a normal healthy man. *Para*-aminosalicyclic acid (PAS), ethambutol (EMB) or capreomycin (CM) were added 48, 24 and 6.5 h before culture stop (whole culture time 72 h). The following drug concentrations (mg/ml) were tested: PAS Na = 0.153; EMB dihydrochloride = 0.028; CM sulfate = 0.015. These concentrations are approximated from calculations based on the therapeutically single daily doses, being 150–200 mg/kg with PAS, 25 mg/kg with EMB and 15 mg/kg with CM. As can be seen from the Table, achromatic lesions (AL), chromatid breaks (B′) and isochromatid breaks (B″) were found. Chromatid translocations (RB′) were completely absent (for description of the aberration types mentioned see ref. [2]). The sum totals of all breaking events per cell (calculated from B′ = 1 and B″ = 2) range from 0.030 to 0.110. These values are not elevated over control values found in our laboratory ranging from 0.0250 to 0.1025 (ref. [3]). Irrespective of the cell cycle stages treated PAS, EMB and CM are inactive with our experimental conditions. Negative results have also been reported with other antituberculosis drugs. INH is inactive in the leukocyte test with concentrations up to 1.0 mg/ml and elevates the frequencies of chromatid aberrations only with the unphysiologically high concentration of 5.0 mg/ml[4]. Rifampicin (RMP) is inactive in the leukocyte test as well as in the *Drosophila* test[5]. Streptomycin (SM) exhibits a strong activity in inducing achromatic lesions (AL) in human chromosomes in vitro[6], an aberration type that should not be taken as an indicator of induced mutations. A prospective controlled clinical trial of patients with pulmonary tuberculosis to test possible chromosomal effects of INH, SM and PAS; INH, SM and EMB as well as INH, RMP and EMB in triple combinations in vivo is in progress.

Zusammenfassung. Die Antituberkulosemittel *Para*-aminosalizylsäure (PAS), Ethambutol (EMB) und Capreomycin (CM) zeigen keine chromosomenbrechende Aktivität an menschlichen Leukozytenchromosomen in vitro.

G. OBE, B. BEEK and K. L. RADENBACH[7]

Institut für Genetik, Freie Universität Berlin, Arnimallee 5–7, D–1 Berlin 33 (Germany), and Lungenklinik des Städtischen Krankenhauses Heckeshorn, Am Grossen Wannsee 80, D–1 Berlin 39 (Germany), 14 June 1973.

1 D. T. ARAKAKI and R. S. SPARKES, Cytogenetics *2*, 57 (1963).
2 G. OBE, K. SPERLING and H. J. BELITZ, Angew. Chem., int. edg. *10*, 302 (1971).
3 G. OBE and J. HERHA, Fortschr. Med. *91*, 533 (1973).
4 H. LÜERS and G. OBE, Newsl. envir. Mutagen Soc. *4*, 36 (1971).
5 E. VOGEL and G. OBE, Experientia *29*, 124 (1973).
6 G. OBE, Molec. gen. Genetics *107*, 361 (1970).
7 We thank Mrs. R. PIEPER for her careful technical assistance.

Zur Klärung des «Trochophora»-Begriffes

Viele Larvenformen wirbelloser Tiere werden einfach als *Trochophora* oder als *Trochophora*-ähnlich etc. bezeichnet, was gewisse Verwandtschaftsverhältnisse vortäuscht und daher häufig sachlich verwirrt. Bei detaillierter Analyse zeigt sich aber vielfach nur eine ökologisch bedingte Übereinstimmung (Bewimperung; vergl. den Begriff «Wurm»), welche morphologisch jedoch keinen Aussagewert enthält[1,2].

Die charakteristische *Trochophora*-Larve ist nicht allein durch prae- wie postoralen Cilienkranz und durch Wimperschopf wie Telotroch, sondern durch Augen, rechtwinkeligen Darm, sich aushöhlende Mesodermbänder und besonders durch Solenocyten (Geisselzelle-Protonephridien, bei Coelomata) gekennzeichnet; sie kommt den meisten marinen Anneliden (Archiannelida, Polychaeta) wie Echiuriden zu (nicht aber den Myzosto-

1 L. v. SALVINI-PLAWEN, Z. wiss. Zool. *184*, 205 (1972).
2 P. FIORONI, Z. wiss. Zool. *182*, 263 (1971).