Abhängigkeit der Durchblutungsgrösse vom Tumorgewicht. Bei Variation des arteriellen Mitteldrucks zwischen 40 und 135 mm Hg steigt die Durchblutung der einzelnen Tumoren linear mit zunehmendem Perfusionsdruck an. Eine zunehmende Rarefizierung der terminalen Strombahn mit ansteigendem Tumorgewicht wird belegt durch eine starke Zunahme des Strömungswiderstandes, der schon bei sehr jungen Tumoren wesentlich höhere Werte als bei verschiedenen Organen aufweist.

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A Study of the Primordial Germ Cells During their Migratory Phase in Steel Mutant Mice

The primordial germ cells (PGCs) of the mouse embryo can first be identified in the caudal end of the primitive streak, allantoic bud and yolk sac splanchnopleure around day 8 of gestation[1–5]. When first detected, the PGCs number about 100. On day 9 they reach the hind gut splanchnopleure and number about 500. On day 10 they reach the dorsal mesentery, mesenteric root and coelomic angles and number about 1,000. By day 11 the gonadal ridges are heavily populated with about 2,000 germ cells[2–5]. The migratory phase of germ cell development appears to end during day 12 at which time they number about 5,000[2]. The germ cells are known to divide along the migration path before infiltrating the gonadal ridges[5].

Mice carrying 2 mutant genes at the Steel (*S1*) locus are sterile, anemic and lack hair pigment[6]. The sterility, which is due to the absence of germ cells in the mature gonad[7,8], may be due to a failure in the proliferative and/or migratory capacity of the PGCs[9].

The present work is a study of mutant Steel mice and their normal littermates to further elucidate the process of primordial germ cell development.

WC/Re – *S1*/+ females and C57BL/6J – *S1*^{d}/+ males were mated overnight. The presence of a vaginal plug at 08.00 h indicated day 0 of gestation. Pregnant females were killed by cervical dislocation exactly 9, 10 and 11 days later (08.00 h). The embryos and surrounding membranes from two 9 day litters, and 4 each of 10 and 11 day litters, were fixed in 95% ethanol, embedded in paraplast (M.P. 50–52 °C) and sectioned at 10 µm.

PGCs are recognized cytologically from their high content of alkaline phosphatase[3]. Sections were stained for this enzyme in Fast Red TR salt coupled to α-Napthyl

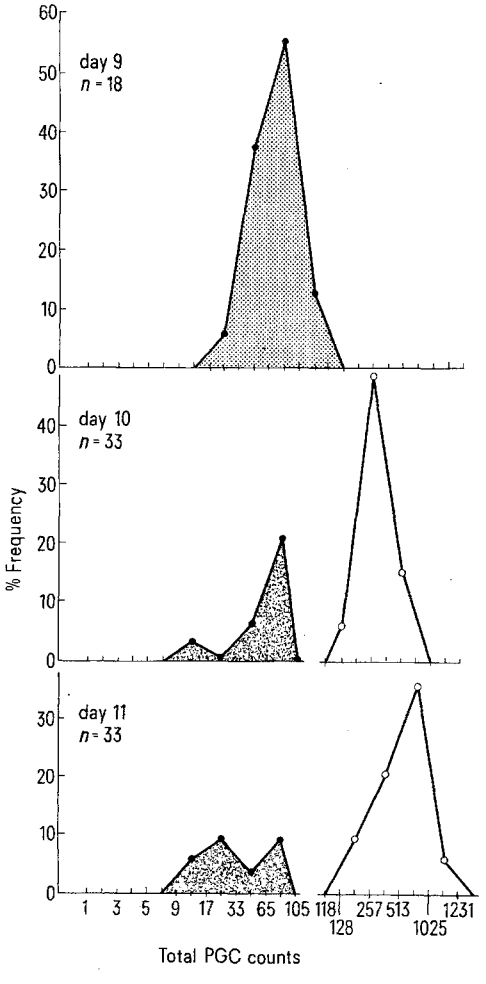

Fig. 1. The percent frequency of total PGC counts arranged on a logarithmic scale, showing a bimodal distribution of PGCs on days 10 and 11.

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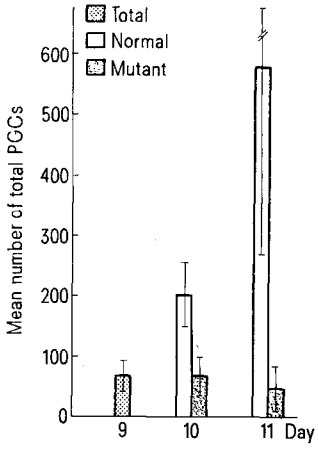

Fig. 2. An increase in the number of normal germ cells is seen on day 10 and 11 whereas the mutant PGCs remain about the same.

Phosphate for 15 min at pH 9.4, and then mounted in glycerine jelly[2]. The PGCs of alternate sections were counted and their locations recorded.

Excluding resorptions, 84 embryos were studied, 1/4 of which were expected to carry the genes *S1/S1^d* and thus express the germ cell defect. Besides the gestational age, each embryo was staged by somite number. Somite counts ranged from 8–17 on day 9, 25–33 on day 10 and 35–43 on day 11. Two embryos of 8 and 11 somites were among the day 10 embryos and thus were classified with the day 9 group for analysis.

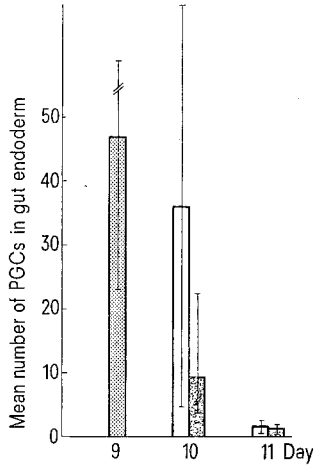

Fig. 3. The decrease in PGCs from the gut endoderm in both mutant and normal embryos indicates an exodus of germ cells from this region after 9 days.

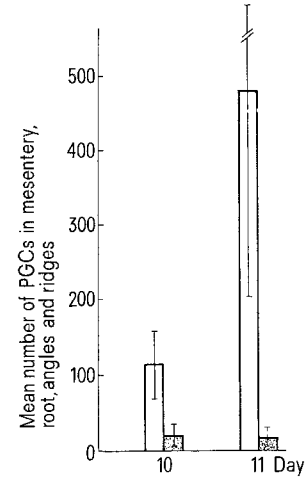

Fig. 4. The infiltration and proliferation of normal germ cells into the dorsal mesentery, mesenteric root, coelomic angles, and gonadal ridges at 10 and 11 days. Mutant PGCs are in these same locations. Few PGCs are in the gonadal ridges on day 10 whereas most are there on day 11.

On day 9, the percent frequency of total PGC counts, as arranged on a log scale (Figure 1), shows that the *S1/S1^d* embryos cannot be distinguished from their heterozygous and wild type littermates. On days 10 and 11, bimodal distributions are evident indicating a segregation within the germ cell population. The number of embryos in the two smaller groups on these days represents 28.8% of the total, which is well within an expected 25% frequency range ($\chi^2 = 0.44$, 1 d.f., $0.5 < p < 0.7$). The germ cell counts found in the smaller groups are presumed to be from the *S1/S1^d* mutants and include all day 10 and 11 embryos having a PGC total of 104 or less.

The means of the day 9 total counts (Figure 2) and the mutant day 10 and 11 counts are not significantly different. However, a dramatic difference exists between the day 9 mean and the means of the day 10 and 11 normal embryos, the two latter representing a 3- and an 8-fold increase respectively.

A reduction in the PGC population from the gut endoderm (Figure 3) is an indication that the mutant germ cells do migrate. In fact, mutant PGCs, although few in number, appear in the same locations on the same days as do normal PGCs (Figure 4). Less than 2% of the normal germ cells reached the gonadal ridges by day 10, whereas after 11 days over 70% populate the ridges. In the mutant embryos, 23% of the germ cells reached the ridges by day 11 and an additional 12% were found in the adjacent mesenteric root and coelomic angles. 44% of the germ cells are located in sites ectopic to the normal path of migration and the remaining 21% are found in the gut mesoderm. Considering that the mutant germ cells do not proliferate it would appear that their rate of migration is comparable to that of normal PGCs. In other words, at least 63% of the PGCs in the normal migratory path will reach the gonadal ridges.

Except for a paucity of germ cells, there was no obvious developmental difference between the mutants and their litter mates from the 9th to the 11th day of development.

The reduced numbers of PGCs in mutant embryos may be due to a failure in proliferation or an excessive rate of cell death. There does not, however, seem to be a deficiency in the capacity of the PGCs of mutant embryos to migrate towards the gonadal ridges[10].

Résumé. Les souris qui sont homozygotes pour la mutation Steel (*S1*) sont stériles, due à l'absence des cellules germinales dans des gonades adultes. Les gonocytes mutants, malgré que leurs nombres sont faibles, émigrent par la voie normale.

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Reverse Diapedesis; the Mechanism of Invasion of Lymphatic Vessels by Neoplastic Cells

The common human cancers kill by metastasis, initially by lymphatic metastasis. Because experimental animal tumours rarely metastasize to lymph nodes the phenomenon of lymphatic metastasis has been little studied. The way in which tumour cells initially penetrate lymphatic vessels is not known. Possible mechanisms include access through major deficiencies in the lymphatic wall or open ended lymphatics, enzymatic destruction of lymphatic endothelium and active cellular movement (diapedesis) between lymphatic endothelial cells.

In a model of lymphatic metastasis described elsewhere[1,2], Rd/3 tumour cells are injected into the rat