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Letter to the Editor

Tumor Homogeneity Largely Determines the Growth of Human Tumour Xenografts in Two Systems*

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IN REVIEWING our experience over the last several years with human tumor xenografts using both nude mice (subcutaneous implantation) and normal mice [the subrenal capsule assay (srca)] [1, 2], we were disappointed with both the apparent take rate (nude mice) and the frequency with which untreated control specimens grew (normal mice). In a group of 21 ovarian tumours, for example, all tumours were implanted subcutaneously; only 8 could be further transplanted. Fifteen explants under the renal capsule were made and in eight of these growth in the untreated control specimens could be demonstrated. Of six testis tumours similarly tested, only 2/6 grew subcutaneously and 2/3 control tumours grew under the renal capsule.

We performed an analysis of two possible factors influencing these results, the history of prior treatment and the histological appearance of the tumour specimen received. When the data were reviewed from the viewpoint of prior therapy (Table 1), it was found that among the eight ovarian tumours 'taking', four had no prior therapy, and of the thirteen not taking, eleven had not been pretreated. For the srca, 6/8 specimens showing growth were obtained from untreated patients, as were 6/7 specimens that failed to grow. For testis tumours, one of the two takes occurred with untreated tumour, and two of the four non-takes were also not previously treated. In the srca of the three untreated tumours, only one showed growth in the control; two failed to grow. No clear relationship could thus be found between a history of treatment and growth.

Histological analysis of the human tumour specimen proved much more fruitful (Table 2). When tumour cells could be identified in more than 50% of the microscopic fields at 100× magnification, growth occurred in the nude mice 8/12 times for ovarian tumours (0/9 tumours with 'negative' histology) and the srca was positive 8/10 times (0/5 from tumours with <50% tumour/field). For testis tumours, 2/4 tumours grew when histology was 'positive' and 0/2 when histology was 'negative'. For the srca, the comparable data were 2/3 and 0/2.

It is clear that while prior therapy has little

Table 1. Analysis of xenograft growth as a function of pretreatment of the human tumour

Total tumours	Pretreated	Not pretreated
Ovarian (21)	6	15
Growth s.c. in nude mice (8/12)	4	4
Growth srca (8/15) normal mice	6	2
Testes (6)	3	3
Growth s.c. in nude mice (2/6)	1	1
Growth srca normal mice (2/13)	1	1

Table 2. Analysis of xenograft growth as a function of the homogeneity of the human tumour specimen

Total tumours	Tumour cells in >50% of 100× microscopic fields	Tumour cells in <50% of 100× microscopic fields
Ovarian (21)		
Growth s.c. in nude mice (8/21)	8/12	0/9
Growth scra in normal mice (8/15)	8/10	0/5
Testis (6)		
Growth in nude mice	2/4	0/2
Growth scra normal mice	2/3	0/2

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effect on the growth of human tumours in these two xenograft models, the adequacy of the tumour specimen largely determined the growth parameters in both systems. Histologic preparations from the subcutaneous tumours in nude mice and from the renal capsule in normal mice all demonstrated tumours, with a minor to major ingrowth of host-responsive cells in the normal mice. That histology may influence the interpretation of growth and response to treatment in the srca in detail is the subject of another paper now in preparation.

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