Several points seem to emerge; first, tumours derived from nodule line D2 seem more capable of inducing cell-mediated stimulation than do tumours from line D1 (4/5 vs. 1/5). Second, although cell-mediated inhibition was seen in three out of eight cases, this effect was seen only in first passage tumours. The tumours lost this capacity with serial passage in unsensitized Balb/c mice. For example, lymphocytes from mice bearing a D1 tumour in first passage gave a 31% decrease in tumour growth *in vitro*; in passage 3, no inhibitory or stimulatory effect, and in passage 4, a 48% increase in tumour growth. This observation suggests the importance of using primary or early passage tumours to detect a cell-mediated inhibitory response. Third, cell-mediated inhibition was only detected with a lymphocyte to target ratio of $10^3:1$; stimulation was detected at ratios of $10^2:1$ or $10^3:1$, although more frequently with the lower ratio; and fourth, cross-reactivity was observed between D1 and D2 tumours, more frequently at doses of $10^3:1$ than $10^2:1$ (Table 3). It has also been seen between D1, D2 and MTV-induced mammary tumours at the higher ratio (unpublished data).

Table 3 Effect of Sensitized Lymphocytes on Syngeneic MTV-free Mammary Tumours Tested against Nonsensitizing Tumours

Sensitizing tumour	Target tumour	No. expts. CMI*		No. expts. Stimulation	
		10:3/1†	10:2/1†	10:3/1†	10:2/1†
D1	D2	2/5	0/8	1/5	3/8
D2	D1	0/2	0/4	2/2	0/4
Total		2/7	0/12	3/7	3/12

* CMI—Cell-mediated inhibition.

† No. of lymph node cells per tumour target cell.

Cross-reactivity suggests the presence of an organ-specific or possibly nodule-specific, rather than tumour-specific, antigen. The presence of organ-specific antigens has been postulated by Weiss *et al.*⁹ on the basis of the ability of lactating mammary gland to immunize against D1 and D2 mammary tumour growth. It is of interest that they also found that pre-immunization led to enhanced growth *in vivo* of D1 and D2 tumours, a situation in keeping with the *in vitro* data reported here.

Preliminary studies show that serum taken from sensitized mice bearing D1 and D2 tumours can sometimes block the stimulation effect (G. H. and D. M., unpublished results). The experiments presented here, however, demonstrate clearly that lymphocytes from tumour-sensitized hosts can show "enhancement" or stimulation of tumour growth. These data support the hypothesis by Prehn that weakly antigenic tumours, in this case virus-free Balb/c mammary tumours (ref 9; and D. M., unpublished results), elicit a cellular immune reaction that stimulates tumour growth. The significance of this phenomenon has important implications for understanding the role of the immune system in neoplasia, and in particular for understanding such phenomena as "sneaking through", immunosurveillance, and the immunological significance of weakly antigenic tumours.

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Chromosome Pairing

IN a useful article which appeared under this title recently¹ H. L. K. W. says at one stage: "Nothing is known about the mechanism of chromosome pairing at the molecular level, but Watson and Crick (*Nature*, **171**, 964; 1953) suggested that it involved the pairing of complementary nucleotide chains to form a double helix. There seems to be no alternative to this account for the specificity of pairing, and a more detailed hypothesis along these lines has been proposed by Sobell (*Proc. US Nat. Acad. Sci.*, **69**, 2483; 1972)".

To me, there at least "seems to be an alternative" in the form of a model in which two homologous double helices of the Watson-Crick type are paired specifically about a dyad axis coincident with their long molecular axes^{2,3}.

A similar mechanism of pairing might also be involved in the formation of tertiary structure in the nucleic acid of chromosomes where repeated, perhaps particularly reverse tandem, base pair sequences occur.

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Diphtheria Toxin: Specific Competition for Cell Receptors

DIPHTHERIA toxin causes the catalytic inactivation of polypeptide chain Elongation Factor 2 when the enzymically active N-terminal fragments of toxin, particularly fragment A, are mixed with broken cells of almost any eukaryotic source¹⁻³ or when complete toxin molecules are incubated with intact susceptible cells⁴. Incubation of intact cells with fragment A does not lead to EF-2 inactivation. Probably, therefore, an apparatus exists in the membranes of susceptible cells that facilitates the uptake of toxin and generation of its fragment A in the cytoplasm and the entry process involves the C-terminal portion of the toxin molecule, fragment B (ref. 5).

Uchida *et al.*⁶ have described the product of a mutant toxin gene, *crm*₁₉₇, a non-toxic protein of the same molecular weight as toxin which has an apparently normal fragment B but an enzymically inactive fragment A. Because *crm*₁₉₇ reduces the effect of toxin on HeLa cells and yet has no effect on the reaction catalysed by fragment A *in vitro*, Uchida *et al.* suggested that *crm*₁₉₇ might compete with toxin for sites on the cell membranes.

We now show by dose-ratio analysis that the inhibition can indeed be described as competitive. Typical HeLa cell dose-response curves for toxin alone and with *crm*₁₉₇ are shown in