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Natural Cellular Defense Activities Against Tumors – Cytostasis and NK Activity*

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Several immunocyte populations are active in the natural cellular defense against tumors. Among these are macrophages [1], natural killer (NK) cells [2], cells mediating antibody-dependent cellular cytotoxicity [3], natural cytotoxic (NC) [4] cells, and natural cytostatic cells [5]. The activities of these cells are directed against membrane determinants which are widely spready on a variety of tumor cells. The NK cells kill mainly lymphoid tumor cells, and the cytostatic activity is directed against adherent tumor cells which originate from solid tumors.

In the present study we describe murine cytostatic activity and several physical and biological characteristics of the spleen cell populations mediating it.

Table 1. Comparison of cytostasis and NK activity

	Cytostasis	NK activity
Adherence (Sephadex G10)	+ and –	–
Phagocytosis	–	–
Thy-1	–	–
Fcγ-receptor	+	–
Activity in:		
10-day-old mice	Fully expressed	Lower than young adults
12-month-old mice	Fully expressed	Lower than young adults
Effect of:		
Incubation at 37 °C	No effect	Activity disappears
Hydrocortisone acetate (in vivo)	No effect (or enhancement)	Decreased activity
Carrageenan (in vivo)	No effect (or enhancement)	Decreased activity
LPS (in vivo)	Increased for longer than 5 days	Increased for 48 h
dsRNA	No effect	Increased activity
Effect of primary tumor bearing:		
Urethan induced	Decreased	No change
DMBA induced	Increased	Decreased
Induced by forced breeding	No change	Decreased

Table 1 summarizes some characteristics of natural cytostatic cells in comparison to NK cells. It can be seen that the only common feature of these two populations is the absence of a thymic (thy-1) antigen and that both types of cells are nonphagocytic.

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Table 2. Fractionation of splenocytes from normal mice according to adherence

	NK activity		
	Unfractionated	Nonadherent	Adherent
% cells in fraction	100	37	7
No. of lytic units/10^7 effectors	30	15	7.5
No. of lytic units/fraction	30	5.5	0.5
	Cytostatic activity		
% cells in fraction	100	37	7
No. of cytostatic units/10^7 effectors	5	5	10
No. of cytostatic units/fraction	5	5	0.7

Table 3. Fractionation of splenocytes from mice bearing primary DMBA-induced tumors according to adherence

	NK activity		
	Unfractionated	Nonadherent	Adherent
% cells in fraction	100	43	9
No. of lytic units/10^7 effectors	0	0	0
No. of lytic units/fraction	0	0	0
	Cytostatic activity		
% cells in fraction	100	43	19
No. of cytostatic units/10^7 effectors	10	2.5	10
No. of cytostatic units/fraction	10	1.1	1.9

Utilizing different adherence properties of NK and cytostatic cells on Sephadex G10 columns murine splenocytes can be separated into a nonadherent population which expresses most of the NK activity and an adherent population which when eluted expresses most of the cytostatic activity (Table 2). Cytostatic cells and NK cells respond differently to the bearing of primary adenocarcinomas and adenoacanthomas induced by the chemical carcinogen dimethybenzanthracene (DMBA). The NK activity in tumor-bearing mice decreases to zero levels while the cytostatic activity increases considerably (Table 3). The data clearly show that there is an enrichment in the cytostatic activity in the adherent cell fraction of tumor-bearing mice.

The fact that the cytostatic activity is boosted in mice-bearing tumors is of much potential interest, and these findings should be extended to other tumor systems including cancer in humans.

References

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