AMITOZYN – AN IMMUNITY REGULATOR

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Use of antitumor preparations while conducting chemotherapy is accompanied by the whole range of complications. The most evident is myelodepressing action of alkylating agents, anthracycline antibiotics, cytarabine, urea derivatives and tacsans. At the same time hemopoiesis inhibition, immunosuppression (as a result of tumor growth, immunosuppression treatment conducting – chemotherapy, hormonal therapy, extensive operative interventions) mainly occur [1].

Capability to reveal mild immunomodulatory action is inherent to the unique anticancer preparation amitozyn. This fact directed us at supposition about its participation in the process of natural immunity regulation, however, the data concerning this direction are limited [2, 3].

Objective of the research was studying of Amitozyn influence on one of the key pleiotropic interleukins – Il-1 synthesis induction.

Materials and methods. We used two-stage method [4] of Il-1 synthesis detection by mice peritoneal macrophages F1(CBAxC57Bl/6). Numerical data were worked out with variational statistics methods.

Research results. Amitozyn influences on IL-1 synthesis by mice peritoneal macrophages F1(CBAxC57Bl/6) in vitro illustrated in the tables 1 and 2. It was found that amitozyn has dose-dependent influence on this complicated biological process.

Table 1

Amitozyn influence on IL-1 production by mice macrophages F1(CBAxC57Bl/6)

Experiment form	Concentration, mkg/ml	IL-1 induction imp/min	*Stimulation index	p<
Control	-	3188±119	-	-
Amitozyn	100	22133±1207	6,9	0.001
	10	9011±347	2.8	0.001
	1	4005±201	1.3	-
	0,1	4746±304	1.5	0.05
	0,01	4330±229	1.4	0.05

Notes: * - stimulation index was counted as radioactivity proportion of the experiment and control.

It was noticed that preparation at dose 100 mkg/ml significantly increases interleukin synthesis stimulation indexes comparing to the control ones. The effect of IL-1 synthesis induction depends on concentration of the preparation (table 1). Usually synthesis stimulation is observed starting with low preparation doses (0.01 mkg/ml), though, the most significant effect is observed at the high concentrations from 100 up to 500 mkg/ml. Such amitozyn doses are commensurable with therapeutic ones in conditions of its use in vivo.

Table 2

Amitozyn influence on IL-1 production by mice macrophages F1(CBAxC57Bl/6)

Experiment form	Concentration, mkg/ml	IL-1 induction imp/min	*Stimulation index	p<
Control	-	847±119	-	-
Amitozyn	500	3520±381	4.1	0.001
	50	2400±307	2.8	0.001

The obtained data confirm that amitozyn stimulates IL-1 production by LPS-activated macrophages. Thus, amitozyn preparation proves to be inductor of IL-1 synthesis in vitro conditions.

Investigations of dose-effect dependence showed that use of low mitogen doses has stimulating action, and high doses – inhibiting action on IL-1 synthesis induction. These facts indicate quite specific, conditioned by certain regulatory mechanisms, preparation action on the immunity system cells and prove the fact of amitozyn immunomodulatory influence on organism.

Conclusion. The conducted researches showed that amitozyn preparation has an influence on IL-1 induction at non toxic for cells doses and therefore can be used in the medicinal treatment of immune-dependent and oncological diseases.

References

1. N.I. Perevodchikova Chemotherapy fundamentals // Moscow, 2000, p.336.
2. L.A. Zaika, O.I. Bolsunova, Y.A. Potopalska, A.I. Potopalsky Amitozyn strengthen the immunity by increasing functional activity of natural killers (NK) //Abstract book First (Inaugural) Ukrainian Congress for Cell Biology, April 25-28, 2004, Lviv. –P.297.
3. L.A. Zaika, A.I. Potopalsky, O.I. Bolsunova, Y.A. Potopalska, Yu. V. Patskovsky The perspectives of application of immunomodulatory properties of antitumor preparation amitozyn in complex treatment of oncological patients // Theses of 1st Ukrainian Research Conference “Domestic antitumor preparations” 14-15th of October, Kyiv, 2004, p. 14.
4. Mizel C.B. Il-1 in T-cell activation//Immunol.Rev.-1982-V.63-P.51-72.