

SPLEEN PEPTIDES ACTIVATE NATURAL KILLER CELLS

Introduction

The described spleen peptide preparation, is used for more than 40 years in supporting tumor therapy as a drug. Numerous pharmacological as well as clinical data show the interaction with the immune system. The immunological effect represents the underlying pharmaco-dynamical principle. (1-10)

The spleen peptide preparation contains standardised oligopeptides by the manufacture process, which are extracted, highly purified and enriched from pig spleen by a special process.

The **NK cells** (natural killer T-cells or Cytotoxic cells) represent a special species of lymphocytes. They possess the ability to identify and damage directly tumor cells. The activation of these cells is a desirable effect of a immunological aligned tumor therapy, because tumor patients frequently show a decreased NK cell activity.(11) It is expected, that by the activation of these cells the tumor cells, existing in the body, can be destroyed, before these begin to form metastases.(11-12)

The available investigations to the spleen peptide preparation indicate the increase of activity of the NK-cells in mice after application of the injection solution.(6)

The data presented here, describe for the first time about an activation of **human** NK cells, after application of the injection solution and/or after incubation with the spleen-peptides.

NK cell activity as diagnostic resources

For the physicians exist the possibility to examine blood tests of the patients on a possible activation of the NK cells, before starting a immunological oriented therapy.

Here the NK cell activity before and after incubation of the lymphocytes of the patient blood with different available immunological active drugs is measured. So it is possible, to evaluate the individual response of the patients on the different immunostabilizing drugs and to optimize the therapy from the beginning.

The determination of the NK cell activity is described in lit. (13-14) Hereby the number of active human cancer cells (K 562) is determined, after incubation with the (pre-treated with the immunological drug) lymphocytes population. As positive control the NK cell activity is determined after incubation of the lymphocytes with Interferon-alpha.

The used concentration of the spleen peptides corresponds to the therapeutic concentration on the basis of the application recommendation (1 mL cont. 30 µg oligopeptide / 5 L blood = 6 ng oligopeptide / mL).

Samples

The available data were provided by the laboratory Dr.Lauk & Dr. Breitling GmbH. 100 results for activation of the NK cells are listed continuously in anonymous form retrospectively, starting from August 1999.

The selection of the patients took place in the order of getting the samples. There was no classification of the respective diagnosis made, because these information were not available. A selection of certain samples took not place.

Results

The aim was to find out, whether the spleen peptide preparation causes a modulation of the NK cell activity.

Therefore, a simplifying classification of the results can be made, which become fair in practice application.

Patients, who exhibit an increase of the NK cell activity of more than 10 %, are called as responder. Patients with a decrease of the activity of more than 10 % are considered as negative responder, patients with a change of the activity up to 10 % as non-responder.

Tab.1 summarizes the results.

It shows, that the largest group consists of patients, in which the spleen peptide injectible solution causes an increase of activity of the NK cells of more than 10 %. Also with view of all samples (inclusive of the negative and non responder) the increase of the NK cell activity by the peptides are statistically significant ($P < 0,001$, t-test for paired samples). The classification into responder groups shows Fig.1.

One could recognize also, that a significant number of patients shows no response. In connection with this, it would be in principle meaningful to examine before beginning of an immunologically aligned therapy, on which active substances the patients at all respond. Obviously plays the individual immunological condition a significant role.

Additional, it is remarkable, that in the negative responder group, with already lower basic activity, the activation cannot be achieved with Interferon-alpha, which is observed in the two other groups.

Classification	number of patients	basic activity (%)	activity after modulation with spleen peptides (%)	activity after modulation with IFN-alpha (%)
responder	48	35,3 (±11,7)	42,6 (±13,2)	49,7 (±12,6, n=28)*
non-responder	45	38,8 (± 8,5)	38,8 (±8,5)	49,4 (±10,5, n=35)
negative responder	7	29,1 (±11,1)	24,1 (±10,0)	35,3 (±9,8, n= 5)
all samples	100	36,4 (±10,6)	39,6 (±11,9)	48,5 (±11,8, n=68)

Tab.1

Assign of the patients to the groups of response as well as the mean of NK cell activity.

Indicated are the average values of the NK cell activity (± standard deviation).

*: The data of positive-controls (modulation by IFN-alpha) were not available with all samples. Stated here is the number of the data of positive-controls.

Clinical NK cell activation

With the diagnostic method described here, one could ask, whether the results are transferable also to the practical application. There is a clinical observation (15), which gives information about that:

39 patients with advanced colorectal tumor are treated postoperatively about 10 days with the spleen peptide injection (1 ml p.d.,i.m.). As control group served 11 patients, who did not receive the peptide therapy. The basic activity of the NK cells was determined with all patients forwards and 15 days after the operation, similar to the procedure described above. The results of the activity measurement shows tab.2.

One can recognize, that the patients profit from the therapy with the spleen preparation. Under the peptide therapy the NK cell activity of the patients in comparison to the control's group can be increased significantly.

	NK cell basic activity before the operation (%)	NK cell basic activity 15 days after op (%)
spleen-peptide-therapy (n=39)	22,1 (±5,3)	26,6 (±6,2)
control group (n=11)	21,1 (±5,4)	19,1 (±6,3)

Tab.2

NK cell activity from patients with colorectal tumor,
before and after operation (± standard deviation).

The difference between the two groups 15 days after the operation is
statistically significant ($P < 0,05$, t-test)

Fig. 1: Division of the patients to the different groups of response (n=100)

Discussion

The available results show, in agreement with the already available pharmacological results, the improving of the NK cell activity by use of spleen peptides. The examination of the NK cell activation before the beginning of the therapy represents here a good diagnostic tool. During the evaluation of the results it should be noted that immunological effects must be always regarded in the general context. A strong influence of individual components does not mean in every case a more competent immune system. A moderate effect which means a stabilization of the immunological network is in each case the best method.

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