VBR 02

A POSSIBLE WAY FOR GENERAL CANCER AND METASTASIS PREVENTION ?

M. von Ardenne and W. Krüger

Tumorimmunology has failed so far to establish a generally practicable cancer immunotherapy. One reason is that biological cancer control is not exclusively based on classical immune reactions. Thus, any attempt to stimulate unspecific defense mechanisms, which often accompany, supplement or even superimpose "specific" defense reactions, must be taken seriously. However, approaches like these are often refused by laboratory scientists and clinicians, because the repeatedly observable surprising over-all effects cannot always easily be attributed to a certain target and their statistical evaluation is often difficult. On the other hand, randomization and double-blind studies must not be the latest tools of medical science. With this dilemma in mind we started our concept of "oxygen multistep immunostimulation" 15 years ago. Its rationale is the combination of biological response modifiers (BRM) with improved oxygen supply. Whereas the effects of BRM can be quantified by established tests, the oxygen effects are hardly demonstrable on laboratory animals. In contrast, the benefit of the oxygen treatment is obvious for man, but here are BRM studies difficult. However, clinical trials with different oxygen/BRM combinations were promising. A retrospective study by Kaiser and Sarembe, Medical Academy Dresden (unpublished) revealed a remarkable reduction of both the death rate and metastasis in cervical carcinoma patients. The results are detailed here.

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VBR 03

ETHNOGRAPHIC-GEOGRAPHIC AND SOCIAL-ECONOMIC CANCER INCIDENCE IN IRAK

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We have studied 25,319 patients (15,300 males and 10,320 females) who were histopathologically diagnosed with carcinoma and classified according to the WHO International Classification of Diseases (ICD). The social-economic and ethnographic-geographic conditions were considered in evaluating the datas and correlated with their analoges in Central Europe.
The inhabitants in southern Irak are social-economically and ethnographic-geographically homogenous. The landscape is flat with dilated marshland, where bilharziasis, predominantly schistosis hematobium is endemic. The majority of the inhabitants have agricultural professions.
In contrary, the population in northern Irak is heterogenous. They have generally lighter skin color than the population in southern Irak. The landscape is hilly with mountains, bilharziasis is rarely observed in northern Irak.
Our study showed bladder carcinoma, with its 13.1% among all the male cancer patients including patients younger than 15 years old, is the most cancer incidence of the male population in southern Irak, whereas among the female population is at the third place with 6.2%
Compared with the northern Irak inhabitants, bladder carcinoma is placed number nine in male population with 3.31% and occured seldom among the female population.
In northern Irak, where the population have generally lighter skin color, cutaneous carcinoma is the predominant cancer incidence for both male and female patients with 21%; basal cell carcinoma is the predominant histopathologic finding. In southern Irak, cutaneous carcinoma is at the third place with 8.1% among male and with 7.5% at the second place among female populations.

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VBR 04

GENETICS OF ONCOGENESIS IN DROSOPHILA MELANOGASTER

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We have found in the fruit fly Drosophila melanogaster 19 recessive mutant genes which are causally related to the development of specific types of malignant neoplasms (Gateff, Science 200, 1446, 1978; Adv.Cancer Res. 37, 1982). The wild-type genes are instrumental in the control of cell division rates and/or differentiation-process in the following embryonic cell-types: (i) the optic neuroblasts, (ii) the blood cells, (iii) the gonial cells and (iv) the imaginal discs, e.g. the primordia of the adult integument in the larva. The mutant genes cause malignant transformation in the above cell-types and, thus, the development of lethal invasive tumors during development in the larva. The mutant genes can be propagated indefinitely. In each generation 25% of the animals in a population are tumor bearing. Temperatur-sensitive alleles have also been obtained with the help of which the time of the wild-type gene activity during development can be identified. At the restrictive temperature in such stocks 100% of the animals show the lethal tumor phenotype. One of the tumor genes lethal(2) giant larvae is cloned and is presently under intense structural and functional investigation on the molecular level (Mechler et al. The EMBO J. 4, 1551, 1985) Six further oncogenes are being analysed cytogenetically with the aim to be cloned.

The Drosophila recessive oncogenes show a causal, one step relation between a mutational event in a particular gene and the malignant transformation of a specific cell-type.

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VBR 05

SUPPRESSION OF ONCOGENIC LETHALITY BY REINTEGRATION OF LETHAL(2)GIANT LARVAE DNA SEQUENCE INTO THE DROSOPHILA GENOME

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Recessive mutations of the lethal(2)giant larvae (l(2)gl) gene of Drosophila melanogaster produce lethal neoplasms of the imaginal discs and the brain hemispheres in the third instar larvae. A chromsomal segment containing the l(2)gl gene has been cloned and was shown to contain a transcription unit which is structurally altered in the 50 different l(2)gl alleles examined. The developmental profile of expression of the two RNAs (6 and 4.5kb) made by this transcription unit coincides with the two major terminal phases of cell proliferation in the developing fly, namely early embryogenesis and the late third instar larvae (Mechler et.al. 1985. EMBO J.,4:1551). Tumors are produced when both normal alleles of the l(2)gl gene are in-activated by deletion or insertional mutation.

Using P-factor mediated transformation, a 12kb DNA segment covering the l(2)gl gene was reintegrated into the germ line of heterozygous l(2)gl/+ flies. Among the progeny, some homozygous l(2)gl deficient animals which normally would have succombed of brain and imaginal disc neoplasia were able to develop into normal and fertile adults. Further transformation using shortened l(2)gl DNA segments allowed to map more precisely the functional limits of the gene. Thus, this experiment demonstrates that the development of neuroblastoma and imaginal disc tumors is the result of impaired l(2)gl gene function. When the function is restored the oncogenicity in the l(2)gl deficient animals is completely suppressed.

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