Division Mechanisms of Tumorigenesis (S0109 / V200)

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* Note: The previous head of the Division Mechanisms of Tumorigenesis as emeritus (1994) was asked by the Management Board to continue under special contract - without DKFZ budget of his personal disposition - certain previous activities: Coordination of the Israel cooperation program of the DKFZ; chairing the nomination committee of the Dr. Emil Salzer-Prize for Cancer Research; advice of external research projects and institutions, especially regarding problems of preventive and/or regulatory toxicology; editorship of various scientific journals, publications of previous experimental results and current investigations in the scientific history of cancer research.

For members of the “Fachbeirat Pharmazie” appointed by the Deutsches Museum, München, the period of this report was a busy phase in advising the Museum for its establishing a new intramural exhibition on the development of pharmacy and biomedicine in the 19th and 20th century [1]. The exhibition covers i.a. important aspects of cancer research and oncology including treatment of cancer diseases. To transmit in an attractive manner current biomedical knowledge to the broad diversity of visitors of the museum, e.g. by mottos such as “You yourself are chemistry”, a broad spectrum of modern multimedia techniques is used. Finally on May 5th, 2001, the exhibition was opened by the Director General of the Museum in a festive ceremony. It will serve as a special highlight in the celebrations taking place on occasion of the 100th Anniversary of the Deutsches Museum in Munich 2003. - The transnational cooperation in cancer research of the Deutsches Krebsforschungszentrum (DKFZ) with research establishments in Israel, executed together with the State of Israel Ministry of Science, Culture and Sport (MOS), is the longest lasting, formalized and worldwide recognized program of external scientific cooperation of the center. Its first 25 years were completed in 2001/2002 in which more than 100 joint cooperation projects were successfully performed. A status report of the current program may be found in [2]. In the present reporting period two information flyers on the cooperation program [3] and on the Modalities for the development of bilateral joint projects between scientists of the DKFZ and of Israel [4] were issued.

Publications (* = external co-author)


Tumor promoters of the environment as risk factors of cancer (S0109-3)

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In the publication of results of experimental investigations main emphasis was laid on the research area above. It comprises qualitative detection and quantitative determination of tumor promoters, especially of the diterpene ester (DTE)-type, in irritant materials utilized in the human environment (in nutrition, in medicinal therapy etc.). - In the nutritional area presence and quantitative determination of certain DTE in milk was investigated further. Moreover, in the area of pharmaceutical drugs out of the general quantitative testing strategy proposed previously (see Hecker 1998, previous reports) for certain medicinal drugs special testing protocols were developed to assess - at low cost and in a quick manner - their putative iatrogenic risk of cancer by content of irritant principles.

According to the general testing strategy proposed, aiming at assessment of anyone irritant materials, a special quantitative testing protocol has to be used comprising a battery of several standardized short term assays. They are based upon the putative mechanism of action of the irritant principles involved, e.g. DTE. The results of such quantitative testing are summarized in what is called the “toxicosis” of the special material. To control the reliability of the prognoses achieved, during the investigational period of protocols, such prognoses are validated experimentally by independent in vivo quantitative testing of the irritant material utilized in the initiation/promotion protocol on mouse skin. The toxprognoses may be used to assess the risk of cancer inherent in the material tested by extrapolation to human exposure, accounting for the actual exposure (therapeutic) dose. Such extrapolation of prognostic results of short term assays is quite analogous to the generally accepted procedures of risk assessment in case of environmental materials suspicious of classical solitary carcinogenic activity. Thus, the toxprognoses are determined for tumor promoters (or conditional cancerogens) according to our general quantitative strategy, i.e. for the alternative second category of cancerogens (Hecker 1998, 1999) may be used in predictive and/or regulatory toxicology as basic reference regarding measures of cancer prevention and/or cancer prophylaxis.
Model of a dietary risk of cancer by irritant materials. In the reporting period the research program P513 operated together with the National Research Center, Cairo, Egypt, was developed further. In Egypt, the green fodder for dairy cattle, for example of goats, often is contaminated by irritant plant species of the genus Euphorbia (spurge family), especially by E. peplus, E. helioscopia and E. nubica. For the case of contamination with E. peplus in mother goats as experimental animals [see, Research Report 2001(1998/99)], it was shown that irritant DTE occurring in the contaminating plant intoxicate the goats and, in addition, show up in their milk. In further trials (continuing this program), mother goats were held on green fodder contaminated with E. helioscopia or E. nubica, respectively [1], given at a dose 30g fodder/day/goat for a period of four weeks. This feeding protocol again led to intoxications of the mother goats. Moreover their suckling kids were intoxicated by the milk of their mothers, to the toxications of the mother goats. Further investigations of the intoxicated milk using microchemical techniques (HPLC) turned out that it contains irritant DTE, i.e. of the ingenane type in case of E. helioscopia and of the tiglane type in case of E. nubica [2]. Hence for all three cases of contamination of the fodder with irritant plants, the milk of the mother goats contained DTE of the same structural type as occurring in the contaminating plant. It is, therefore, indicated to determine the toxprognoses of milk of this provenience in a special quantitative testing protocol according to our general strategy above, to assess the actual cancer risk involved with its consumption. An appropriate special quantitative testing has been developed for the first time for homöopathic drugs (see below).

Model of an iatrogenic risk of cancer by irritant materials. In ethnomedicines of developing countries for a variety of different medicinal indications, frequently medicinal treatment by plant preparations is recommended, including toxic species e.g. of the spurge and mezereon plant families (India [3], Africa, China). Also, in Western countries medicinal use of a great many plant preparations is well known since centuries (phytomedicine, complementary medicine). In the last decade, such preparations have become especially popular, mostly because of the naive and erroneous expectation that preparations “directly form God’s Pharmacy” (e.g. Maria Treben, “Gesundheit aus der Apotheke Gottes”) are devoid of unwanted side effects and provide solely beneficial efficacies. For pharmaceuticals often used in Germany in the popular “homöopathy”, so-called “mother tinctures”, are manufactured at large scale. For legal access of homöopathic drugs to the pharmaceutical market according to the German Arzneimittelgesetz of 1986 (AMG 86), the producer is required to prove just their quality: since homöopathy in the AMG 86 is earmarked as “a special form of therapy” (“eine besondere Therapierichtung”). In contrast to allopathic drugs, homöopathic drugs are not required to prove both drug safety and drug efficacy. This “generous” exemption by AMG 86 (also valid for two other “special forms of therapy”) is not accepted at the European level (European Pharmacopoea). Therefore, in the near future, producers of drugs will be required to prove also for homöopathic drugs in addition to quality, their safety and efficacy (and for the drugs of the other “special forms of therapy”). To meet this increase of official requirements in the reporting period, according to our general testing strategy for homöopathic drugs special quantitative testing protocols were developed and investigated as to their feasibility for assessment of a putative risk of cancer by mother tinctures of spurge and/or mezereon origin. A certain standardized special testing protocol for these drugs was made up which provides reproducible and reliable toxprognoses by its asset of short term assays. This is the first time to show that our general quantitative strategy of testing irritant environmental materials may be used as a lead to develop testing protocols appropriate for assessment of the cancer risk of many more irritant environmental materials [4,5]. In case of homöopathic drugs they cover drug safety; however, therapeutic efficacy continues to remain a matter of patients believe.

Publications (* = external co-author)


