EDITORIAL

Can Risk Assessment and Chemoprevention Research Rely on Surrogates for Tumour Yield?

The main areas of interest within toxicological pathology relevant to cancer prevention are risk assessment, mechanisms of carcinogenesis and chemoprevention. All rely to a large extent on studies in experimental animals. In the present issue of the APJCP, Subapriya and Nagini (2003) report on the chemopreventive potential of an ethanol extract of neem leaves in rats, providing evidence of reduction in gastric tumour yield as well as diminished lipid peroxidation within lesions and change in antioxidant parameters in background tissue. The paper thus provides a good example of a study encompassing both mechanisms and preventive potential. Fukushima et al (2003) earlier argued for the necessity of taking mechanisms into account in assessing hazard risk with animal models and many of their points are pertinent to a wider ongoing debate regarding the applicability of surrogate end point biomarkers (SEBs).

In a recent issue of Cancer Epidemiology Biomarkers and Prevention a point/counterpoint discussion of this theme was included. While Armstrong et al (2003) concluded only limited usefulness of SEBs, Kelloff and others (2003) argued for high utility in the development of cancer chemopreventive agents against sporadic cancers. Clearly, distinction can be made between those biomarkers which are actual focal lesions with some potential to give rise to cancers and others which reflect processes underlying neoplastic development (see Moore et al., 1999, Ito, 2000 and Brewer et al., 2001, for further discussion of this point). Typical examples of each are listed in the Table.

We are now in a position to identify very early lesions in many of the organs of the body which are important in terms of human cancer burden, using either morphological characteristics, histochemistry or immunohistochemistry. Furthermore, a number of techniques are available to assess oxidative stress and proliferation at the cell level, as well as necrosis and single cell death, termed oncosis and apoptosis, respectively (Moore, 2000). However, none of these latter are specific and the conclusions which may be drawn from information on such mechanism-based SEBs cannot be given the same weight as quantitative or qualitative data on lesions actively involved in the histogenesis of tumours. Unfortunately, it is not possible at the present to determine exactly which preneoplastic foci will progress to malignancy, but for experimental purposes they can be argued to provide the best parameters presently available.

In addition to their use for relatively short-term or medium-term assessment of chemopreventive potential, facilitating screening of large numbers of candidate compounds, very early focal lesions induced by carcinogens be applied to address the thorny question of whether dose-dependence is a straight line phenomenon, even at the very low exposure levels prevalent in the human situation. The glutathione S-transferase P form positive focus in the rat liver has proved particularly helpful for dose-response studies of hepatocarcinogenesis (Tsuda et al., 2003) and has allowed a good deal of evidence to be generated in favour of thresholds with both genotoxic and non-genotoxic chemicals.

Recognizing the necessity to promote discussion of how animal models may best be employed to address questions of risk assessment and identification of promising candidate agents for chemoprevention, especially in foodstuffs, the APOCP has organized satellite symposia to be held in Bangkok, Thailand on the 15th and 16th of November (see Scientific meetings in the present issue). Originally planned

Table. Range of Preneoplasia-based and Mechanism-based Surrogate Endpoint Biomarkers

Preneoplasia-based surrogate endpoint biomarkers (P-SEBs)
Quantitative data for preneoplastic lesions (e.g. H&E staining/ GST-P immunohistochemistry)
Kinetic data for preneoplastic lesions (e.g. proliferation/apoptosis)
Phenotypic data for preneoplastic foci (e.g. histopathology/enzyme or molecular phenotype)
Genotypic data for foci (e.g. mutations of growth control genes)
Mechanism-based surrogate endpoint biomarkers (M-SEBs)
Quantitative data for tissue kinetics (e.g. proliferation/mitoinhibition/apoptosis)
Status for DNA damage or oxidation stress (e.g. adduct formation/lipid peroxidation)
Serum hormonal milieu (e.g. insulin/estrogen/testosterone levels)

to coordinate with AsiaTox III, this latter has now been postponed, necessitating a change. The symposium is now scheduled to follow the Thai National Cancer Conference. It is to be hoped that sufficient scientists will nevertheless be able to participate to allow in depth discussion of alternatives to the long-term rodent carcinogenicity study for assessment of hazard potential as well as the advantages and disadvantages of animal models for detection of chemopreventive agents. Sine the focus is on Asia, coverage of some of the most promising ingredients of foodstuffs in the different countries of the region will also be included. We hope to see you there.

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EDITORIAL MESSAGE

Appearance and Disappearance of the UICC Logo from the Cover of the APJCP - Apologies and an Explanation

On the cover of Vol 4 No 2 of the APJCP the logo of the UICC was newly included along with the statement that the APOCP was affiliated with the International Union Against Cancer (UICC). The express permission of the UICC had been obtained for this purpose, but the APJCP has now been informed that such use of the logo breaches the contract that exists between the UICC and Wiley Press, the publishers of their official journal, the International Journal of Cancer. Why this was earlier overlooked by the Geneva office of the UICC is unclear, but the APJCP is naturally complying with their request that the logo no longer appear on our cover. As Managing Editor, I would like to apologise for the confusion and ensure that any scientist who made a subscription to the APJCP on the basis of the apparent affiliation is welcome to cancel with complete reimbursement of their subscription.

Dr Kazuo Tajima, Chairman of the APOCP, is also Project Leader for Epidemiology for the UICC and he and one of his predecessors, Dr Kunio Aoki, have done their utmost to highlight the activities of the UICC in the pages of the APJCP (Aoki, 2000; Tajima and Moore, 2002). To promote the common goals of the UICC and APOCP, Dr Tomoyuki Kitagawa, Chairman of the Japanese UICC National Committee, prevailed upon the Geneva office to provide US $10,000 in support of APOCP activities. Acknowledgement of this assistance is made in the APOCP website, which has been improved with some of this grant to allow all papers published in the journal to be downloaded as pdf files. Regional meetings of the APOCP now carry the statement that they are held partly under UICC auspices and here there is no problem with display of the logo. This is the background to the changes made to the cover.

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