SECOND INTERNATIONAL SYMPOSIUM
ON
HORMONAL CARCINOGENESIS

IN ASSOCIATION WITH THE
CENTER FOR NUTRITIONAL TOXICOLOGY
THE KAROLINSKA INSTITUTE (NOVUM, SOUTH CAMPUS)

JULY 5-9, 1994
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Featured on this issue’s cover of Cancer Research are Dr. Nobuyuki Ito and his colleagues at Nagoya City University, Japan, who have been active in the field of experimental carcinogenesis for many years. Concentrating first on the histogenetic aspects of and then defining the sequences of lesions involved in the pathogenesis of cancer of the liver, urinary bladder, stomach, kidney, and large intestine, this group has contributed a great deal of information on carcinogenic and modulating agents.

The work for which Dr. Ito is perhaps best known, however, is in the area of risk assessment, and especially for his research of the risk potential of food additives. Considerable attention has been devoted to antioxidants, which are widely used in foodstuffs, medicines, and cosmetics, because of their action in preventing the oxidation of lipids. Butylated hydroxyanisole (BHA) is a particularly important example of a useful food additive, generally considered safe, and lacking mutagenic or carcinogenic potential. In fact, BHA has been thought of as a good candidate for chemoprevention, because it inhibits the carcinogenic process in several animal models.

However, in 1982–1983, Dr. Ito and his coworkers published clear evidence of BHA carcinogenicity in the forestomach of F344 rats (Gann, 93: 332, 1982; J. Natl. Cancer Inst., 70: 343, 1983), which provoked great controversy concerning the interpretation of the effects of antioxidants on carcinogenesis. The most remarkable impact of their BHA findings on the world of risk assessment is reflected in the achievement of a consensus that regulatory actions should be decided after thorough examination of both the benefit and the risk of the chemicals. The fact that consideration of the relative benefits of the chemicals is now more vigorously advocated is directly related to the Ito group’s documentation of BHA carcinogenicity as a function of dosage and its intrinsic mechanisms of action.

Subsequently, this collective has concentrated its efforts on the modifying potential of numerous other antioxidants, both synthetic and naturally occurring. Thus, in many instances, they have found that beneficial and disadvantageous actions can be exerted simultaneously in different tissues. Based on the experience of BHA, Ito and his colleagues have also extended their studies of carcinogenicity to other antioxidants, such as catechol, caffie acid, sesamol, and hydroquinone. One finding of particular note was that catechol, a natural antioxidant used widely in industry, induces glandular stomach adenocarcinomas in F344 rats (Jpn. J. Cancer Res., 81: 207, 1990; Adv. Cancer Res., 53: 247, 1989).

With considerable expertise in the carcinogenic process in several organ systems, Dr. Ito and his associates are now primarily occupied with the problem of risk assessment of the large number of man-made agents being introduced into the environment. They have, therefore, focused on the development of a reliable medium-term bioassay for detecting carcinogens and modifiers. Named the “liver medium-term bioassay for carcinogens,” the resultant protocol has been established as particularly useful for the initial safety assessment of environmental carcinogens (Carcinogenesis (Lond.) 9: 387, 1988; CRC Crit. Rev. Toxicol., 19: 385, 1989; Food Chem. Toxicol., 30: 979, 1992). Recently, they have also successfully developed a new “multigang carcinogenesis bioassay” system, which can detect carcinogens or modifiers in various organs within the same animals [Carcinogenesis (Lond.) 13: 1513, 1992; Cancer Res., 53: 32, 1993]. The findings that have been generated to date bear a good relationship to known results from long-term, conventional carcinogenesis assays.

Acting as a team, but with each member concentrating on different organs, they are continuing their efforts to develop and improve animal models for such important human neoplasms as prostate, urinary bladder, kidney, stomach, and intestine, as well as liver carcinomas. The aim is to provide reliable aids with which to investigate the mechanisms underlying human neoplasia and approaches to chemoprevention in each organ. These models have already contributed to research into human cancer control. The prostate cancer model using 3,2‘-dimethyl-4-aminobiphenyl, established by Katayama et al. (J. Natl. Cancer Inst., 68: 867, 1982) and perfected by Dr. Ito’s group, is, for example, now one of the most appropriate systems for studying human prostate cancer (Cancer Res., 51: 1264, 1991).

Pictured are Nagoya City University staff members, from left to right, Drs. Katsumi Imaida, Tomoyuki Shirai, Nobuyuki Ito, Masao Hirose, and Ryohei Hasegawa. We are indebted to Dr. Takashi Sugimura for background material and illustrations.

Sidney Weinhouse