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Carcinogenic risks in the high-risk groups

Dai Nakae, Masakazu Takahashi, Midori Yoshida, Fumiyuki Uematsu and Akihiko Maekawa*

Department of Pathology and *Director, Sasaki Institute, Sasaki Foundation

Environmental chemicals are involved in the development of a majority of human cancers. It is thus very important to detect and evaluate their carcinogenic risks and to elucidate the underlying mechanisms, which have been being investigated epidemiologically for humans and basically using animals. Regarding the latter, however, there is a problem that most of the animal studies have dealt with high doses of chemicals, and as a result their low dose effects directly applicable to human situations still remain largely obscure. On the other hand, many human cancer cases have been indicated to occur under the specific "high-risk" conditions, such as chronic viral hepatitis for liver cancers, chronic gastritis due to *Helicobacter pylori* for gastric cancers, chronic infectious or non-infectious inflammation on respiratory tracts for lung cancers, cholelithiasis and chronic inflammation on bile tracts for bile tract cancers, chronic cystitis and bladder stones for bladder cancers and chronic hormonal imbalance for cancers in the endocrine and genital systems. The common feature of such conditions is that chronically continuing, low-impact stimuli induce states in which carcinogenic processes are stimulated. Behaviors of many chemicals may be different under such states form those under the ordinary conditions. It is thus uneasy to estimate risks for chemicals for people in the high-risk groups from those in the no- or low-risk groups. In this context, we have been investigating the carcinogenic risks and mechanisms of chemicals at both high (carcinogenic in animals) and low (environmental for humans) dose levels in the animal models with some similarities to known human high-risk situations in comparison with those under the intact animals. For the studies, we have been using the model of hepatocarcinogenesis under the chronic liver injuries in male Fishcer 344 rats fed a choline-deficient, L-amino acid-defined diet and that of uterocarcinogenesis under the chronic hormonal imbalance in female Donryu rats initiated with *N*-ethyl-*N*'-nitro-*N*-nitrosoguanidine. In addition, we are developing new animal models to be used. While these our studies are all under progress, we would like to introduce some preliminary data in this symposium to propose the audience to understand the importance of carcinogenic risks of environmental chemicals in the high-risk groups.