

---

## MEETING REPORT

---

# Daiyukai Medical Research Institute 25th Anniversary - Symposium for 'Medium-term Carcinogenicity Assays'

To commemorate the 25th anniversary of the founding of Daiyukai Medical Research Institute, a symposium was held in the Hotel Castle Plaza in Nagoya, Japan, on the 30th of January. Attended by some 300 scientists and

representatives from industry and government Ministries, the theme 'Medium-term Carcinogenicity Assays' covered rat liver and multi-organ examples as well as transgenic mice, all of these being accepted as alternatives to long-term in

### Symposium Contents

Speaker: <b>Akihiko Maekawa</b> , Sasaki Institute 'Opening remarks'	Chairperson: <b>Masae Tatematsu</b> , Aichi Cancer Institute
<b>Seiko Tamano</b> , Daiyukai Institute 'Development and utilization of medium-term models'	<b>Hiroyuki Tsuda</b> , National Cancer Center
<b>Tomoyuki Shirai</b> , Nagoya City University 'A medium-term rat liver bioassay for rapid <i>in vivo</i> detection of carcinogenic potential'	<b>Akihiko Maekawa</b> , Sasaki Institute
<b>Shoji Fukushima</b> , Osaka City University 'Multi-organ medium-term models for <i>in vivo</i> detection of carcinogenic potential'	<b>Michihito Takahashi</b> , Peer Review Center
<b>Samuel M Cohen</b> , University of Nebraska 'Transgenic mice as alternative models for carcinogenicity testing'	<b>Makoto Asamoto</b> , Nagoya City University
<b>Toshiro Nakagaki</b> , Ministry of Health, Labour and Welfare 'Food chemical safety requirements'	<b>Katsumi Imaida</b> , Kagawa University
<b>Michihito Takahashi</b> , Peer Review Center 'Summary of the symposium'	



**Speakers and Chairpersons for the Symposium**

vivo assays for carcinogenicity testing at the Fourth International Conference on Harmonization of Technical requirements for Registration of Pharmaceuticals for Human Use, held in 1997 (ICH-IV). This is of particular importance given the continuing debate on the necessity for consideration of mechanisms in risk assessment.

In the opening address, Akihiko Maekawa introduced the concept of cancer attributability to environmental carcinogens. He also covered the history of the development of the *initiation* and *promotion* theory which is the rationale for medium-term models. With reference to ICH-IV he stressed the timeliness of the present symposium to maintain progress in this area.

Seiko Tamano, of Daiyukai itself, then gave an overview of the field, pointing to the essential division of carcinogens into DNA-reactive genotoxic and non-genotoxic types and the need for appropriate models to distinguish genetic from epigenetic modes of action. He also provided a synopsis of the results already obtained with the medium-term rat liver and multi-organ bioassays.

Further details of the 'Ito' medium-term liver model were provided by Tomoyuki Shirai, who concentrated attention on the good correlation observed between long-term and medium term findings. Shoji Fukushima similarly emphasised the advantages which can accrue from application of the multi-organ approach for assessment of carcinogenic and promoting potential in the medium-term.

The benefits and pitfalls with use of transgenic animals demonstrating elevated sensitivity to carcinogens were introduced by Samuel Cohen. Examples used for illustration included the rasH2, heterozygous p53 and homozygous xeroderma pigmentosum (XPA) strains. The limited utility for evaluating mechanistic considerations for extrapolation to humans was emphasized.

The viewpoint of the Ministry of Health, Labour and Welfare of Japan was eloquently presented by Toshiro Nakagaki, concentrating attention on the inherent complexity of decision-making and the requirement for detailed information from a comprehensive package of tests.

Finally, before the toasts and refreshments, Michihito Takahashi gave the audience the benefit of his long years of experience of research in testing for regulatory purposes in succinctly summarizing the proceedings. He also presided over a special question session allowing members of industry a voice to help clarify areas which particularly need further attention.

The development of the medium-term models by Daiyukai Institute is the result of a unique long term collaboration between academic scientists working in a University environment and an industrial concern active in

ensuring a healthy living environment. I personally feel that the APOCP should play a greater role in promoting such mutually beneficial contacts between the academia and industry, whether in identification of carcinogenic agents or chemopreventive agents, so that we can effectively work together to promote cancer prevention. For this reason a further meeting is now planned as a Satellite to AsiaTox III, to be held in Bangkok in August (see Meetings Announcements in this issue). I hope to see you there.

### **Malcolm A Moore**

APOCP Coordination Director, APJCP Managing Editor  
c/o Chemotherapy and Experimental Pathology Division,  
National Cancer Center Research Institute,  
1-1 Tsukiji 5 chome, Chuo-ku, Tokyo 104-0045, Japan  
Tel +81-3-3542-2511, Fax +81-3-3542-3586  
e-mail: malcolm812@yahoo.com