

## The 1992 Jsaae Annual meeting

A. SATO

*Tokyo Medical and Dental University, President of the 6th Annual Meeting of JSAAE*

*Yushima 5-45, 1-Chome, Bunkyo-ku, Tokyo 113, JAPAN*

*TEL 03-3813-6111, FAX 03-3814-5971*

The sixth Annual Meeting of the Japanese Society of Alternatives to Animal experiments (JSAAE) was held on December 17 and 18, 1992 at the National Education Center in Tokyo. The meeting was chaired by Dr. Atushige Sato, professor of Tokyo Medical and Dental University and was organized by the organizing committee consisted of Drs. T. Murano, K. Inui and T. Hongo.

The issues of alternatives to animal experiments is of a great concern to researchers as well as educators of life sciences, as witnessed by the annually increasing number of participants. In the Sixth Annual Meeting, there were as many as 700 participants from Japan and abroad.

The Annual Meeting consisted of one plenary lecture, four sessions of symposium and 40 topics of free communications.

Dr. J.M. Frazier of the Johns Hopkins Center for Alternatives to Animal Testing gave the plenary lecture entitled "What is validation and why are we so concerned about it", and discussed the current situation involving the definition of validation, procedure and criteria for evaluation.

Four topics were chosen from the area of toxicology for the symposia. Six lectures were presented at Symposium I with the theme of "Prediction of *in vivo* toxicity from *in vitro* testing". Dr. Frazier discussed "*In Vitro/In Vivo* Extrapolation". Drs. T. A. Donnelly, S.D.S. Braa, I.D. Kidd and G.K. Naughton (Advanced Tissue Sciences, Inc.) "Toxicity and irritation prediction using a three-dimensional human skin model", Drs. T. Tsuchiya, Y. Ikarashi, H. Hata and A. Naka-

mura (National Institute of Hygienic Sciences and Scientific Research Foundation) "Comparative Studies of the toxicity of biomaterials in cytotoxicity test and *in vivo* tissue irritancy test", Drs. K. Ueno, T. Takezawa, Y. Mori, A. Miyashita, K. Endoh and T. Satoh (Chiba University and W.R. Grace & Co.) "An alternative to the hepatotoxicity testing using multicellular spheroids composed of rat liver cells", Drs. J. Kawakami, M. Shimokawa, K. Yamamoto, Y. Sawada, A. Asanuma, K. Yanagisawa and T. Iga (University of Tokyo and Tsurumi University) "Prediction of drug induced adverse reactions to CNS based on *in vitro* studies-convulsant interaction between new quinolone antibacterial agents and non-steroidal anti-inflammatory drugs", and Dr. J.M. Tesh (Life Science Research) "Embryo Culture-Can it be used as a predictor of teratogenicity". Dr. Frazier reported that in order for an *in vitro* testing method to become more than an adjunct method in risk assessment, a technique to extrapolate from *in vitro* model to *in vivo* situation was necessary, and presented his views on the scientific basis for extrapolation.

Eight lectures were given at Symposium II with the theme of "Standardization of *in vitro* cytotoxicity testing". Dr. T. Sofuni (National Institute of Hygienic Science) discussed "Factors affecting the results of *in vitro* toxicological tests", Drs. H. Torishima, R. Yamamoto, T. Nishino, and M. Watanabe (Kurabo Industries and Nagasaki University) "Effect of cell type and serum on cytotoxicity test of chemicals", Drs. Y. Kuroda, H. Kojima, H. Konishi and K. Tamai (Azabu

University, Nippon Menard Cosmetic Co., Ltd. and Institute of Health Science) "Evaluation of combined toxic effects of two chemicals", Dr. M. Inaba (Japanese Foundation of Cancer Research) "Kinetic analysis of cell-killing action of antitumor agents and its application to screening of antitumor agents", Drs. N. Tanaka and K. Sasaki (Food and Drug Safety Center) "Standardization of cytotoxicity assay for medical devices and cosmetic products", Drs. Y. Ohno, T. Kaneko, T. Kobayashi, T. Inoue, Y. Kuroiwa, T. Yoshida, J. Momma, A. Fujii, M. Masuda, T. Itagaki, T. Endo, K. Ohkoshi, J. Okada, H. Kakishima, H. Kojima, K. Takano and A. Takanaka (National Institute of Hygienic Science, Japan Cosmetic Industry Association, Yokohama City University and Showa University) "First phase validation plan of the *in vitro* eye irritation tests for cosmetic ingredients", Drs. A. Nakamura, T. Tsuchiya and Y. Ikarashi (National Institute of Hygienic Sciences) "Standardization of cytotoxicity test for biomaterials", Drs. N. Kobayashi and T. Ueda (Dainippon Pharmaceutical co., Ltd.) "Usefulness and standardization of cell culture system, At present state and in future". Dr. Inaba discussed analysis of cell-killing actions of carcinostatic agents into which pharmacodynamics or pharmacokinetics were introduced. His discussion drew attention of the audience since this is generally disregarded in the field of cytotoxicity tests even though kinetic analysis is important for cytotoxicity tests. Dr. Nakamura explained the cytotoxicity tests (colony assay) described in Japanese Guideline for Toxicity Testing for Medical Materials and Devices that was published recently, pointed out that the colony assay was more sensitive than the agar overlay method and correlated well with local irritancy in the implantation test. He requested peer reviews on the guideline.

In Symposium III, eight lectures were presented with the theme of "Strategies for establishment of new alternatives for target organ toxicity". Professor T. Kamataki (Hok-

kaido University) and his colleagues reported on "Establishment of cell lines which express cytochrome p-450, Professor T. Kuroki (University of Tokyo) "Immortalization of human cells", Dr. Y. Kuroyanagi (Kitasato University) "A Cytotoxicity test using a composite cultured skin), Drs. S.R. Slivka, T.A. Donnelly and G.K. Naughton (Advanced Tissue Sciences Inc.) "Testosterone metabolism in an *in vitro* skin model, Dr. T.W. Class (Organogenesis Inc.) "A human skin model", Drs. T. Hongo, N. Sawada, H. Kimura, K. Sato and A. Sato (Tokyo medical and dental University) "Nephrotoxicity testing using cell culture system", Drs. M. Namba and Y. Gu (Okayama University) "Cytotoxicity assay using human liver cells", Drs. T. Hayashi, H. Itagaki, U. Tamura and S. Kato (Shiseido) "Development of a prediction system for eye irritation considering membrane destruction factor and protein denaturation factor". In developing cell lines by applied genetic engineering, Dr. Kamataki introduced cDNA of cytochrome p450 and NADPH-P450 reductases into CHL cells and obtained cells with high sensitivity (300 times more of the original CHL cells) to aflatoxin B<sub>1</sub>. This is because aflatoxin B<sub>1</sub> becomes epoxy and is activated by the gene transfected p450 and reductase required for its electron transfer. He said that established cell lines hardly had drug metabolizing enzymes and the toxicity of chemicals requiring metabolic activation would be overlooked. By transfection of drug metabolism related genes, toxicity can be detected at a concentration lower than that at which cells non-specifically show toxicity in screening of carcinogens, thereby proving useful for predicting toxicity in humans. This suggested that the gene transfected cell lines would become the mainstream of cytotoxicity tests.

Three lectures were given at Symposium IV with the theme of "Non-biological alternatives". Professor M. Hirobe (University of Tokyo) discussed "Molecular design of artificial cytochrome p-450 and its application to drug metabolism", Professor Y. Murakami

(Kyusyu University) "Drug metabolism mediated by artificial enzymes", Dr. M. Nakadate (National Institute of Hygienic Sciences) "Toxicity prediction of chemicals using structure-activity relationships". Professor Hirobe synthesized p450 mimics with a great potential as an alternative for the artificial enzyme and discussed their possibilities as an alternative means in drug metabolism. Dr. Murakami presented an example of constructing artificial enzymes by combining synthetic bilayer vesicles and vitamin B6 or vitamin B12, and current conditions of researches on diverse drug metabolisms using artificial enzymes. The study on drug metabolism using artificial enzymes is most meaningful not only because it would use less number of animals for isolation of unknown metabolites but also because the use of artificial enzymes would facilitate isolation and refining of the trace metabolism products which is currently expected to be difficult.

All free communications were presented as poster exhibitions and included 14 on eye and skin toxicity, 11 embryo toxicity and teratogenicity, four on phototoxicity and seven on other subjects.

Dr. B. Ekwall (Uppsala University) and his colleagues presented prediction of acute lethal toxicity in man based on rodent LD<sub>50</sub> values and *in vitro* cytotoxicity values under the MEIC Project in which 80 laboratories of the world participated. They reported interesting data that combination of the data on

cytotoxicity and toxicokinetics in humans give a better prediction for human lethal toxicity than the data obtained from rodent LD<sub>50</sub> data.

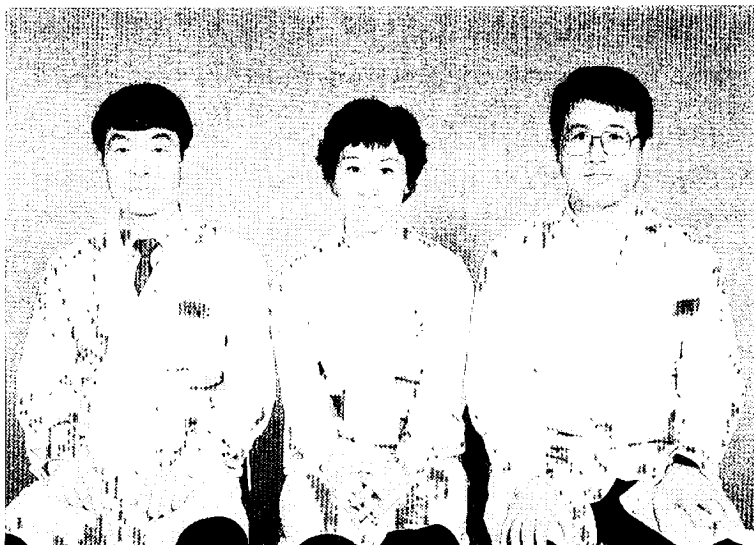
Among the presentation in free communications the most prominent two were selected to the Golden Presentation Award by anonymous votes of the Selection Committee. Presentations by Drs. M. Sugiyama, H. Itagaki and S. Kato (Shiseido Safety and Analytical Center) and Drs. H. Kojima, A. Hanamura, A. Sato, H. Konishi and I. Yoshimura (Nippon Menard Cosmetic Co., Ltd. and Science University of Tokyo) were selected for Golden Presentation Awards. Their articles will be published the next issue in this Journal.

Researchers as well as educators in the field of life sciences must view alternatives to animal experiments as human experimental technique rather than a mere research technique. The 1992 Annual Meeting mainly focused on the future visions of the research techniques of the alternatives.

Finally I would like to express my gratitude to many companies, foundation and other organizations which donated us generous financial supports for the Sixth Annual Meeting of JSAAE.

The next Annual Meeting will be held on December 16 and 17, 1993 at Osaka International Exchange Center with Professor Takashi Tanimura (Kinki University) acting as president.

The Golden Presentation Award at the 6th annual meeting of  
Japanese Society of Alternatives to Animal experiments.



Drs. M. Sugiyama (Center), H. Itagaki (Right) and S. Kato (Left) of Shiseido Safety and Analytical Research Center, who have presented "Prediction of phototoxicity by red blood cells hemolysis test and yeast growth inhibition test"



Drs. H. Kojima (Left), A. Hanamura, A. Sato and H. Konishi (Center) of Nippon Menard Cosmetic Co., Ltd. and Dr. I. Yoshimura (Right) of Science University of Tokyo, who have presented "Prediction of Draize rabbit eye irritation test on the battery system of 7 alternatives to animal tests"