

THE FIFTH ANNUAL MEETING OF JSAAE (1991)

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The annual meeting of the Japanese Society for Alternatives to Animal Experiments counts 5th in this year 1991, and was held in Hadano City on 13-14 of November, 1991. The meeting was chaired by Hiroshi Ono, Director of Hatano Research Institute, Food and Drug Safety Center, which is located in Hadano City, and the meeting was organized and conducted by the executive committee consisted of major staffs of Hatano Research Institute.

In spite of the fact that Hadano is located some 80 km to the west of Tokyo and most participants must have traveled over 1 hour by train from Shinjuku, and that the members of JSAAE then were not more than 250, well over 540 participants have gathered to attend the two-day meeting for scientific communication. The meeting took place at Hadano Municipal Cultural Hall, and proceeded in an auditorium and consequently in an exhibition hall, both of suitable size for this meeting.

The participants have gathered from industries of cosmetics, pharmaceuticals, pesticides and other chemicals, as well as academic and governmental institutes and toxicological testing laboratories. Government officials responsible to regulation of chemicals for the safety were invited, and those from Ministry of Health and Welfare, Ministry of International Trade and Industry and from Agency for Scientific Technology have been attended the meeting. The meeting was also well attended by participants from abroad, being quite an international meeting. Two invited lectures were given and four sessions of symposium were conducted in the auditorium,

and all the 37 free communications were presented as poster exhibition. The posters were shown for a full daytime and a 1-hour due period for discussion was scheduled before noon.

The effort of the meeting was focussed on the alternative research in toxicological field especially on the technological concerns. Four symposia have been planned to inform the audience on the technological concerns. Four symposia have been planned to inform the audience on the state of the art in each field and to discuss newer approaches to safety assessment. This policy resulted, on the contrary, in excluding discussions on ethical, political or practical issue, which was intentionally determined by the organizing committee.

The keynote lecture was addressed by Dr. Yuzo Hayashi, Director of the Biological Safety Research Center, National Institute of Hygienic Sciences. He stated on the basic concept of the alternative research in relation to toxicological aspects of chemical safety. He stressed the importance of validation of test procedures and sensible application of alternative methods as screening, adjunct or replacement to animal experiments. Dr. Hayashi also pointed out the needs for the philosophy to speculate the total figure of human toxicity by integrating the fractionated knowledges obtained with *in vitro* test systems such as isolated or cultured organs, tissues and cells, and organelles. In addition, Dr. Hayashi made a comment that he actually was not yet a member of JSAAE, and gave his high appreciation of this open-mindedness of the society. Indeed, as he said, the alternatives research in this country needs much to be inspired from

neighboring disciplines especially from toxicology for securing the safety of the modern civilized life dependent on chemicals possibly based on the alternative test methods.

Dr. Björn Ekwall of Uppsala University, who has been a leading personality of Scandinavian activity of MEIC, the International Multicenter Evaluation of *In vitro* Cytotoxicity Testing, was invited to give a lecture on the MEIC activity. In this project multiple laboratories have been gathered internationally to test reference chemicals with their *in vitro* toxicological methods, and the data obtained are analyzed using human toxicity data as the reference. Validation of *in vitro* toxicity testing methods has become a major problem of JSAAE, as well as in other scientific bodies committed to the alternative research. Several laboratories from Japan have been engaged in participating in this project.

The first symposium was on "New Experimental Methods of Genotoxic Tests", chaired by Dr. Toshio Sofuni, Division of Genetics and Mutagenesis, National Institute of Hygienic Sciences, and four speakers have presented their lectures; Dr. Minoru Sawada (Hokkaido University) reported their success in "Transfection of cytochrome P-450 cDNA into cultured mammalian cells and establishment of mutagen-sensitive cell lines"; Dr. Kiyoshi Sasaki (Hatano Research Institute, Food and Drug Safety center) reported their "Development of oncogene-transfected cells for assay of tumor promoters"; Dr. Brian Myhr from Hazleton Washington, Inc., Maryland, USA, showed "*In vivo* mutation assay system using *LacZ* transgenic mice"; and Kazuya Mikamo (Asahikawa Medical College) talked on "Interspecies *in vitro* fertilization system to measure human sperm chromosomal damages".

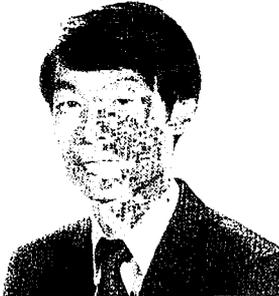
The second symposium was on "Cultured Hepatocytes in Toxicological Studies", chaired by Prof. Akira Ichihara of Institute of Enzyme Research, University of Tokushima. Five presentations were made preceded by an introductory overview of the chairman; Dr.

André Guillouzo from Hôpital Pontchaillou, Rennes, France, Dr. Yasuo Ohno of National Institute of Hygienic Sciences, Prof. Tetsuo Satoh of Chiba University, Dr. Terumoto Kohira of Toyo Jozo Co., and Dr. Yasushi Yamazoe of Keio University. Discussion was focused on the drug-metabolizing enzyme activity of cultured hepatic cells, which is known to change differently by the enzyme according to the culture condition. As for its application to toxicity testings, various endpoints have been proposed such as activities of P-450 (Dr. Ohno) and esterases (Dr. Satoh), or lipid levels (Dr. Kohira). While Dr. Guillouzo reported his challenge in the maintenance of drug metabolizing capacity of cultured hepatocytes, Dr. Yamazoe reported their research on *in vitro* expression of cytochrome P-450 under hormonal influences. Among studies on *in vitro* organ toxicity, that of hepatic cells seems most prominent, although it is obvious that the study needs further investigation, and that various approaches should be attempted simultaneously since the liver has so much multiple functions.

The third symposium entitled "*In vitro* Testings for Developmental Toxicity: Application to Risk Assessment", was chaired by Prof. Kohei Shiota (Kyoto University) and Dr. Ryujiro Shoji (Institute for Developmental Research, Aichi Prefectural Colony). As remarkable progress has been achieved in this field, the topics featured researches over wide range of methods; embryos and larvae of *Xenopus laevis* frog by Dr. Michiko Sakamoto (Kinki University), micromass culture system by Dr. Toshie Tsuchiya (National Institute of Hygienic Sciences), preimplantation embryos of the rat by Dr. Tetsuji Nagao (Hatano Research Institute, food and Drug Safety Center), cultured cells derived from human embryo by Dr. Shinji Nito (Tanabe Seiyaku Co.), and an organ culture system of fetal mouse palates by Dr. Tsuneo Kosazuma (Kyoto University).

The fourth symposium was on the most

Awardees of “Golden Presentation” in 1991 at the 5th Annual Meeting of Japanese Society of Alternatives to Animal Experiments



Toshikatsu Hayashi¹ (upper left), Hiroshi Itagaki² (upper right), Shinobu Kato² (lower left) and Uhei Tamura¹ (lower right) of ¹Shiseido Product Research Center and ²Shiseido Safety and Analytical Research Center, who have presented “Quantitative Evaluation to Predict the Eye Irritation Using Hemoglobin” (see page 227 in this issue).



Akane Kurokawa (left), Takashi Kobayashi (center) and Fumio Ariyuki (right) of Safety Research Laboratory, TANABE SEIYAKU Co., Ltd., who have presented “Cardiovascular Malformations Induced by Phenobarbital and Caffeine in Chick Embryos” (see page 218 in this issue).

salient issue of all the alternative researches, "Alternatives to Local Irritancy Testings", chaired by Dr. Masami Watanabe (Yokohama City University, Nagasaki University at present), featuring four speakers. Dr. Tadao Ohno (Institute of Physical and Chemical Research) talked of "Analysis of cytotoxicity with an enzymatic marker", stressing a high-sensitivity of LDH method. Besides cytotoxicity studies using various parameters of cell injury, two newer approaches to analyze cellular functional responses were introduced; Dr. Atsuo Miyagawa (Hamamatsu University School of Medicine) showed "Measurement of intra-cellular ion distribution in single living cells" using photochemical probes for pH, K^+ , Na^+ , Ca^{2+} and Mg^{2+} , and Dr. Henry Wada (Molecular Devices Corp., Menlo Park, Calif., USA) presented "Measurement of cellular responses using a silicon microphysiometer", which showed a potential method to assess cellular reversibility from irritation injury. Finally Dr. Shoichiro Sugai (Kumiai Chemical Industry) presented their achievement in "A quantitative structure-activity relationship analysis in approach to primary eye irritation of chemicals in rabbits."

Furthermore, free communications by poster presentation exhibited various activities on alternatives to testing methods in genetic, developmental and reproductive, sensitizing and photosensitizing as well as irritating toxicity. Among many informative reports the most prominent two were elected to "Golden Presentation Award" by mutual vote of the participants; Toshikatu Hayashi and his colleagues (Shiseido Safety and Analytical Re-

search Center) presenting "Quantitative evaluation to predict the eye irritation using hemoglobin", and Akane Kurokawa and her colleagues presenting "Cardiovascular malformations induced by phenobarbital and caffeine in chick embryos". These awardees are featured and their articles will be published next issue in this Journal.

Thus, although it was a small-size meeting of two-day communication, the meeting was well be said successful, owing much to the devoted participants. Exciting scientific communications have been achieved among multiple disciplines. The cooperation is still in its early phase in Japan between alternative research scientists and toxicologists. Though needless to say the alternative research has its roots in animal welfare principles, this movement should not be restricted to simple argument against animal experiments by mere sentimentalism of personal or massive levels. The scientists have gathered holding their sympathy with the animal welfare principle. Finally, kind financial contributions from many supporters should be acknowledged. Especially, The Cosmetology Research Foundation has kindly provided a grant for invitation of scientists from abroad.

The next annual meeting will be held in Tokyo under the presidency of Prof. Atsushige Sato (Tokyo Medical and Dental University) in late fall of 1992, where further advances in alternative research will be communicated and more will be discussed including those from philosophical or bioethical aspects.