The 8th International Symposium on Chromosomal Aberrations

– Bridges from past to future,
from hazard identification to risk assessment,
from population to individual, especially children –

October 4–6, 2007

Awaji Yumebutai International Conference Center,
Hyogo, Japan

8th ISCA 2007, Awaji

The 8th International Symposium on Chromosomal Aberrations

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http://www.pac.ne.jp/isca8/

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B. Teh	*M. Hayashi*	*N. Tanaka*
N. Asano	*H. Tanabe*	*M. Honma*
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Co-organized by:

Mammalian Mutagenicity Study Group
Van Andel Research Institute

Awaji Yumebutai International Conference Center
Awaji Island, Hyogo, Japan

General Information

Venue: Awaji Yumebutai International Conference Center
Yumebutai, Awaji-Shi, Hyogo 656-2306, Japan
TEL: 0799-74-1020 FAX: 0799-74-1021

8th ISCA website: http://www.pac.ne.jp/isca8/

Language: The official language of the conference is English.
Simultaneous translation will not be provided.

Registration: Awaji Yumebutai International Conference Center, 2F
Reception Hall (B)
Oct 4 (Thu) 12:00 ～ Oct 6 (Sat.) 12:00

Registration Fees:

Early registration (by May 31, 2007)

General	JPY 20,000
MMS Group Member	JPY 10,000
Student	JPY 8,000
Accompanying person	JPY15,000

Late registration (by August 31, 2007)

General	JPY 25,000
MMS Group Member	JPY 10,000
Student	JPY 8,000
Accompanying person	JPY15,000

On-site

General	JPY 30,000
MMS Group Member	JPY 10,000
Student	JPY 8,000
Accompanying person	JPY15,000

*All payments must be made in Japanese Yen.
**Registration fee includes conference documentation and book of abstracts, as well as access to the lectures, welcome mixer, banquet, and the poster sessions.
***Accompanying person fee covers banquet fee.

Conference Badge: Conference badge will be given at the registration.
Please put on the badge all the time in the conference rooms and social programs.

Internet: If you have your own laptop computer, free Internet access via wireless LAN is available in the Foyer of the conference center. You are also free to use computers in Business Center (B1F). The Westin Awaji Island Hotel has also modems (limited number) and you could use freely in your rooms. Please ask the Westin Awaji Island Hotel's reception desk.

Luncheon Seminar (Sponsored by Amway Japan Limited and Nutrilite Health Institute):
October 5 (Fri.), 12:00-13:15

Travel Desk (JTB): JTB helps you to make arrangements for domestic travels during and after the conference.

Business Hours	Oct 5 (Fri.)	9:00 ～ 18:00
	Oct 6 (Sat.)	9:00 ～ 12:00

Social Programs

Welcome Mixer: October 4 (Thu), 19:00 ～ 21:00
Awaji Yumebutai International Conference Center, 2F
Reception Hall (B)
You could also visit Tea Ceremony House (4F) for some beverages.

Banquet: October 5 (Fri.), 19:15 ～ 21:15
The Plants Museum of Miracle Planet

Excursion: October 6 (Sat.), 13:00 ～ 18:00
Kyoto: Kiyomizudera（清水寺）
(World Cultural Heritage by the Unesco; selected in 1994)
Kiyomizudera stands in the wooded hills of eastern Kyoto and offers visitors a nice view over the city from its famous wooden terrace. Below the terrace, you can taste the spring water, which gives the temple its name and which is said to have healing power.

Drink Service: Drink Service will be provided during the coffee break.

Accompanying persons Program:
October 5 (Fri.) 10:00 ～ 17:00
Hokudan Earthquake Memorial Park
When the Great Hanshin Awaji Earthquake hit this area on January 17, 1995, an active fault of 10 kilometers appeared in the earth. The Park preserves and displays the fault as it was to visitors.

Himeji: Himeji Castle（姫路城）
(World Cultural Heritage by the UNESCO; selected in 1993)
Himeji Castle is widely considered Japan's most spectacular castle. Unlike many other Japanese castles, Himeji Castle was never destroyed in wars, earthquakes or fires and survives in its original form. The castle is famous for its brilliant white exterior and its confusing maze of paths leading to the main keep.

Oral Presentation (Invited Speakers)

Presentation should be made in English.

Only LCD projector will be available. Please note that we will not have a projector for overhead transparencies or 35mm slides. Speakers are requested to bring their own laptop computer and AC adaptor (applicable to Japanese plug outlet: AC 100V 60Hz) for presentations. Your PC should have display output interface with D-sub 15 pin. If your PC has a special display output interface (especially for Macintosh PC), please bring an appropriate display port adaptor. Your laptop computer needs to be tested for presentation at least 1 hour prior to the beginning of your session at PC Preview Corner located in Reception Hall (B). We strongly recommend to bring CD or USB memory to back up for PC troubles.

For those who cannot bring their own laptop, we will provide a conference PC (Windows XP) for presentations. In this case, please bring your PowerPoint file on a CD or USB data stick to PC Preview Corner no later than the day before your presentation. PowerPoint 2003 (Windows) will be available on the conference PC. Please ensure that your presentation is compatible with these versions.

Poster Presentation

1. Poster session venue and date

Poster sessions will be located at hoyer of the Reception Hall (B)
on the 2nd Floor of the Conference Center.

Poster session will be held on 13:15 ～ 15:00 on October 5.

Please keep the poster be presented during the conference.

2. Poster board

Poster should be prepared in English only.

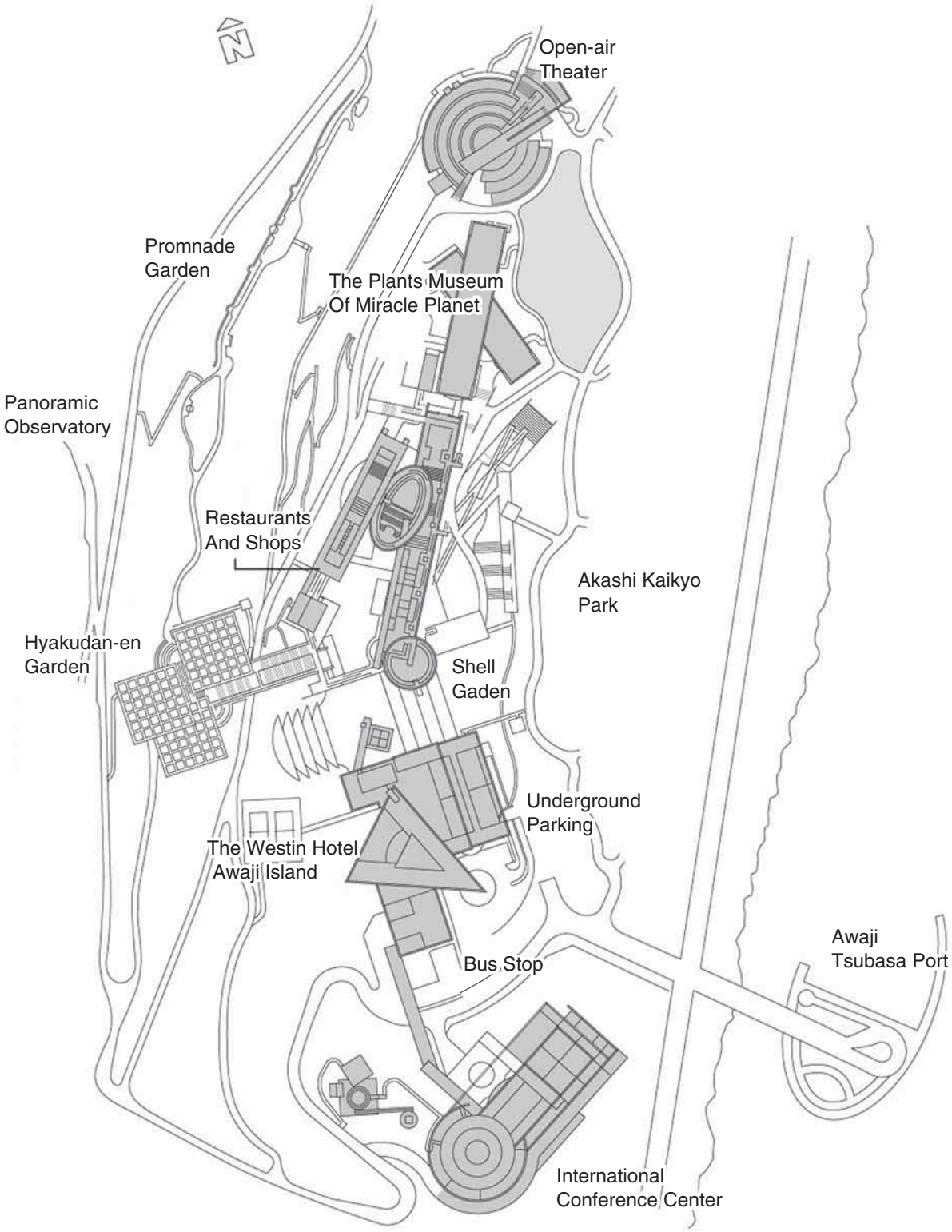
Poster board will be provided with the following dimensions: Height 180cm × Width 90cm. Upper left corner is for the poster number (20cm height × 20cm width), and this space should be unused. Each poster presentation must have a title (20cm height × 70cm width) including authors' names, and affiliations. Authors preparing presentation material on one sheet will have a maximum of 160cm (height) × 90cm (width) in which to make their presentation. Poster numbers will be provided by the Secretariat. Photocopies, illustrations and charts should be prepared in advance, as materials for these purposes will NOT be available on site.

3. Set up / Removal times

Set up	Before Oct 5 (Fri.)	13:00
Removal	Before Oct 6 (Sat.)	13:00

Displays should be set up and removed preferably according to the times listed above. Posters not removed during the allocated times will be dismantled by the Secretariat. The conference organizers cannot be held responsibility for author materials left behind after removal time.

Awaji Yumebutai



Program

October 4

12:00～13:00 **Registration**

13:00～13:15 **Opening address** *M. Hayashi*

13:15～14:15 **Keynote lecture (1)** *Chair: G. Obe*

KL-1 DNA repair and chromosomal alterations
A.T. Natarajan

14:15～15:45 **Symposium (1)** ***Cytogenetic epidemiology*** *Chair: J. Tucker*

S1-1 Biomarkers of chromosomal damage in human populations and risk of cancer
S. Bonassi

S1-2 Why does lymphocyte chromosome damage predict cancer risk?
H. Norppa

S1-3 Fetal exposure to ionizing radiation does not induce persisting chromosomeaberrations in hemato-lymphoid cells
N. Nakamura, M. Nakano, Y. Kodama, K. Ohtaki, J.B. Cologne, E. Nakashima, O. Niwa, M. Toyoshima

15:45～16:15 **Coffee break**

16:15～18:15 **Symposium (2)** ***Children/clinical/germ cell*** *Chair: I.D. Adler*

S2-1 The use of SNP (Single Nucleotide Polymorphism) array in detecting copy number and submicroscopic constitutional chromosome aberrations in solid tumor and patient DNA
B.T. Teh

S2-2 Tumors in the offspring by germ cell exposure to radiation and chemicals in mice: possible relationship to induced genetic changes
T. Nomura, L.Y. Li, H. Nakajima, T. Hongyo, R. Baskar, S. Adachi, H. Ryo

S2-3 Developmental and transplacental genotoxicology
A. Fučić, M. Gamulin, J. Katić, Z. Herceg

S2-4 Chromosome aberrations in mouse embryos and fetuses produced by assisted reproductive technology
H. Tateno

18:15～19:00 **Hotel check-in**

19:00～21:00 **Welcome mixer**

Awaji Yumebutai International Conference Center 2F, Reception Hall B

October 5

09:00～09:45 **Keynote lecture (2)** *Chair: H. Tanabe*

KL-2 Chromosomal and nuclear genome architecture —An evolutionary perspective
S. Müller

09:45～10:00 **Coffee break**

10:00～12:00 **Symposium (3) *Technology*** *Chair: Y. Ishii*

S3-1 Towards the production of humanized model mice using chromosome engineering
M. Oshimura, Y. Kazuki, H. Hoshiya, Y. Kai, S. Abe, M. Takiguchi, Y. Iida

S3-2 Micronucleated CD71-positive reticulocytes: A cross-species bridging endpoint
S.D. Dertinger

S3-3 Radial positioning of chromosome territories: Development of peripheral and interior pooled DNA probes for detecting the disordered nuclear architecture and environment
H. Tanabe

S3-4 Live cell imaging of chromosome segregation processes in multicolor
K. Sugimoto, K. Senda-Murata, S. Oka

12:00～13:15 **Luncheon seminar** *Chair: N. Tanaka*

Sponsored by Amway Japan Limited and Nutrilite Health Institute

LS-1 Genome health nutrigenomics and nutrigenetics: Nutritional requirements for chromosomal stability and telomere maintenance at the individual level
M. Fenech

LS-2 Dietary Supplementation for Genome Stability: Evidence from Recent Controlled Clinical Trials
M. Lemay

13:15～15:00 **Poster session**

P-01 Chromosome tests in clonally proliferated T lymphocytes in vitro from A-bomb survivors do not suggest presence of genetic instability
K. Hamasaki, Y. Kodama, Y. Kusunoki, E. Nakashima, N. Takahashi, N. Nakamura, K. Nakachi

P-02 Possible impact of clonal structure of human lymphocytes in retrospective cytogenetic biodosimetry
Y. Kodama, M. Nakano, K. Ohtaki, A. Noda, N. Nakamura

P-03 No persistence of chromosome aberrations in mice irradiated in utero or soon after birth
M. Nakano, Y. Kodama, K. Ohtaki, E. Nakashima, O. Niwa, M. Toyoshima, N. Nakamura

P-04 Dose-rate effects for dicentrics and translocations with accumulated dose in long-term irradiated mice with low-dose-rate gamma-rays
K. Tanaka, A. Kohda, T. Toyokawa, K. Ichinohe, Y. Oghiso

P-05 Role of Cytogenetics Evaluation in Hazard Classification of Chemicals
T. Morita, S. Sasaki, M. Hayashi, K. Morikawa

P-06 Involvement of hydrogen peroxide on chromosomal aberration induced by green tea catechins in vitro and its implication for risk assessment.
A. Kobayashi, R. Ogura, O. Morita, N. Nishiyama, T. Kasamatsu

P-07 Contents of micronuclei in cultured human lymphocytes
G. C. M. Falck, H. Järventaus, H. Metsälä, L. Heikinheimo, H. K. Lindberg, A. Hirvonen, H. Norppa

P-08 Detection of micronucleated cells and gene expression changes in glandular stomach using mice treated with stomach-targeted carcinogens
E. Okada, Y. Fujiishi, N. Yasutake, W. Ohyama

P-09 Zoxamide – An Antimitotic Fungicide: Application And Assessment of Different in Vitro-Metabolism Systems to Investigate a Potential Metabolic Modulation of Antimitotic Activity
E. Fabian, H. Kamp, G. Damm, S. Triebel, J. Döhmer, M. Akiyama, M. Osawa, R. Landsiedel, B. van Ravenzwaay

P-10 High-resolution genomic analysis of immortalized human cells and human tumor cells using array-based comparative genomic hybridization.
A. Kohara, M. Takeuchi, K. Takeuchi, Y. Ozawa, A. Ohtani, N. Hirayama, S. Shioda, H. Makino, M. Terai, A. Umezawa, H. Mizusawa

P-11 Isolation of mitomycin C -induced micronuclei by laser-assisted microdissection
J. Catalán, H. K. Lindberg, G. Falck, I. Heilimo, T. Hienonen-Kempas, S. Saarikoski, H. Norppa

P-12 CGH and SNP Arrays; as New Tools for Detailed Analysis of Chromosome
T. Suzuki, Y. Luan, D. Prabha, M. Kogi, M. Honma, T. Koizumi, S. Tanabe, Y. Sato, K. Suzuki, T. Yamaguchi

P-13 PKU-β/TLK1 regulates myosin II activities, and is required for centrosome separation and chromosome segregation
M. Hashimoto, T. Matsui, K. Iwabuchi, T. Date

P-14 Characteristics of karyotype abnormalities including Robertsonian translocations in mouse embryonic stem cell lines used in Japan
A. Sugawara, K. Goto, T. Sofuni, A. Takakura

15:00～16:30 **Symposium (4) *Chromosome instability*** *Chair: M. Honma*

S4-1 Targeted and non-targeted induction of chromosomal rearrangements after exposure to ionizing radiation
W.F. Morgan

S4-2 Genomic instability caused through breakage-fusion-bridge (BFB) cycle in human cells
M. Honma

S4-3 Fanconi anemia and chromosomal instability
A. Lyakhovich, J. Surralles

16:30～16:45 **Tea break**

16:45～18:45 **Symposium (5) *Miscellaneous abnormality*** *Chair: M. Fenech*

S5-1 Loss of ChlR1 causes cohesion defects and aneuploidy
A. Inoue, J.M. Lahti

S5-2 Formation of chromatid breaks: Models and mechanisms
P.E. Bryant

S5-3 Disorders in chromosome assembly: New chromosomal aberrations associated with human congenital diseases
T. Ono, R. Kimura, S. Mizuno, K. Yamada, S. Sonta, N. Wakamatsu

S5-4 The prediction of chromosomal effects and their mechanism of induction in Derek for Windows
R.V. Williams, M. Hayashi

19:15～ **Banquet**

October 6

09:00～09:45 **Keynote lecture (3)** *Chair: J.T. MacGregor*

KL-3 The micronucleus assay — Past, present, and future
M. Hayashi

09:45～10:00 **Coffee break**

10:00～12:00 **Symposium (6) *Regulatory aspects — from hazard identification to risk assessment*** *Chair: T. Sofuni*

S6-1 Potential artefacts of the in vitro chromosomal aberration assay
D.J. Kirkland

S6-2 Towards improving the accuracy of genotoxicity testing
S.M. Galloway

S6-3 The dose makes the poison — and the genotoxicant
J.T. MacGregor

S6-4 The Use of Chromosomal Aberration Data in Support of Regulation of Chemicals in Canada
D.H. Blakey

12:00～12:15 **Closing remarks** *G. Obe*

KL-1

DNA Repair and Chromosomal Alterations

A. T. Natarajan

Department of Agroboplogy and Agrochemistry, University of Tuscia, Viterbo, Italy

All mutagenic agents induce lesions in the cellular DNA and they are repaired efficiently by different repair mechanisms. Unrepaired and mis-repared lesions lead to chromosomal alterations. It has become evident that chromosomal instability is obne of the most fore running process in carcinogenesis, as originaly proposed by Boveri in early 90|'s. Depending upon the mutagenic agents involved, diffrernt DNA repair pathways, such as nucleotide excision repair (NER), base excision repair (BER),non-homologous end rejoining (NHEJ), homologous recombinational repair (HRR), cross link repair (FANC), single strand anealing (SSA) etc.,are operative. Following ionizing radiation, DNA double strand breaks (which are considered to be the most important leasion leading to observed biological effects) are repaired either by NHEJ and/or HRR. We have investigated the relative role of these two repair pathways leading to chromosomal aberrations using Chinese hamster ovary (CHO) mutant cells deficient in one of these two repair pathwatys NHEJ operates both in G1 and G2 phase of thye cell cycle , wheras HHR operates mainly in S and G2 phase of the cell cycle. In NHEJ deficient mutant cells irradiated in G1, unrepared DSBs reaching S phase are repaired (unexpectedly with a large mis-repair component) by HRR. In HRR deficient mutant cells, unrepaired DSBs reaching S phase are repaired by NHEJ (unexpectedly with a low mis-repair component) as evidenced by the frequencies of chromatid type of aberrations. Employing a similar approach, following treatment with BPDE, the active metabolite of benzo(a)pyrene, NER and HRR seem to be the most important repair pathways protecting against chromosomal damage induced by this agent. In the case of acetaldehyde, (primary metabolite of alcohol invivo) a DNA cross-linking agent, HRR and FANCO pathways are important for protection against damage induced by this agent. The relative importance of different repair pathways in bestowing protection against DNA damage leading to chromosomal alterations wiil be discussed.

(The project is financialy supported by University of Tuscia, EU Food Safety Programme (DIEPHY), Philip Morris USA and Philip Morris International)

KL-2

Chromosomal and nuclear genome architecture – an evolutionary perspective

Stefan Müller

Department Biology II, Human Genetics, Ludwig-Maximilians University, Munich, Germany

To date, approximately 100 mammalian species were investigated by cross-species chromosome painting. Further, large insert cloned probes have been used for the establishment of high-resolution comparative FISH maps and for a detailed analysis of evolutionary breakpoints. The resulting chromosomal homology maps provided insight into the evolutionary history of each human chromosome. More recently, large-scale genomic imbalances between human and no-human primates interspecies were revealed by arrayCGH, which, together with comparative sequencing efforts, highlighted hotspots of evolutionary genome plasticity and instability. Moreover, this knowledge has been prerequisite to address open questions concerning evolutionary conserved principles of higher order nuclear architecture and its possible consequences on the direction of chromosome evolution.

This lecture provides an overview of recent technological developments in primate comparative cytogenetics and genomics and gives a reconstruction of the major landmarks in primate karyotype evolution. Further, recent results obtained from the analysis of evolutionary breakpoints and from comparative studies of nuclear architecture are presented in the context of human genomic disorders.

KL-3

The micronucleus assay: Past, present, and future

Makoto Hayashi

Division of Genetics and Mutagenesis, National Institute of Health Sciences,
1-18-1, Kamiyoga, Setagaya-ku, Tokyo Japan
E-mail: hayashi@nihs.go.jp

Genotoxicity plays an important role in the safety evaluation of chemicals. It is well known that there are *in vitro* and *in vivo* assay systems with different endpoints for evaluation of chemical genotoxicity. One of the major endpoints is the structural and numerical chromosomal aberration. To assess the induction of chromosomal aberrations by chemicals *in vivo*, the rodent micronucleus (MN) test using haematopoietic cells has been most widely and frequently used. The historical aspects of development of the rodent MN test and the characteristics of the test will be reviewed, then the current development of the MN test and future perspectives of the assay will be summarized and discussed.

Historically, haematopoietic cells have been targeted in cytogenetic studies. Accordingly, the MN test used immature bone marrow erythrocytes as a target cell population. After the introduction of reticulocytes in peripheral blood to be used as a target cell population as effective as bone marrow cells, the applicability of the assay incorporated into other toxicological studies has been expanded. Now the incorporation of the MN assay into general toxicological study has been discussed at the working group for international harmonization of pharmaceutical drug testing. To overcome the limitation of the chromosomal aberration induction assessment at the target tissue of carcinogenicity of chemicals, methods to assess MN induction in other than haematopoietic cells, e.g., liver, skin, intestine and testes, have been developed; much of this work has been overseen by the Mammalian Mutagenicity Study group (MMS).

Another development of the MN assay is an automated system to evaluate MN induction by image analysis and flow cytometry based on a simple endpoint, which is one of the characteristics of the assay. Especially using flow cytometry, a large number of cells can be analyzed and theoretically very small increments in MN frequency can become statistically significant. This issue is important when the outcomes of the assay are used for risk assessment of chemicals and we have to construct a strategy of how to use genotoxicity information in chemical risk assessment for human life. This issue also coincides with discussion of threshold of genotoxicity – especially with genotoxic carcinogens – for risk assessment based on consideration of mode of action.

LS-1

Genome Health Nutrigenomics and Nutrigenetics: nutritional requirements for chromosomal stability and telomere maintenance at the individual level

Michael Fenech

CSIRO Human Nutrition, PO Box 10041, Adelaide BC, South Australia 5000
Email: michael.fenech@csiro.au, Telephone +618 8303 8880, Fax +618 8303 8896

It is becoming increasingly evident that (a) risk for developmental and degenerative disease increases with more DNA damage which in turn is dependent on nutritional status and (b) optimal concentration of micronutrients for prevention of genome damage is also dependent on genetic polymorphisms that alter function of genes involved directly or indirectly in uptake and metabolism of micronutrients required for DNA repair and DNA replication. Development of dietary patterns, functional foods and supplements that are designed to improve genome health maintenance in humans with specific genetic backgrounds may provide an important contribution to a new optimum health strategy based on the diagnosis and individualised nutritional prevention of genome damage i.e. Genome Health Clinics. The presentation will review (a) research relating to the use of the cytokinesis-block micronucleus cytome assay for determining nutritional requirements for prevention of chromosome damage, (b) evidence for the link between micronucleus and nucleoplasmic bridge formation and cancer risk in humans and (c) provide some initial insights on the likely nutritional factors that may be expected to have an impact on maintenance of telomeres.

Program Table

	October 4	October 5	October 6
9:00		**Keynote lecture (2)** Dr. S. Müller (Chair: Dr. H. Tanabe)	**Keynote lecture (3)** Dr. M. Hayashi (Chair: Dr. J.T. MacGregor)
10:00		Coffee break	Coffee break
11:00		**Symposium (3)** Technology Dr. M. Oshimura Dr. S.D. Dertinger Dr. H. Tanabe Dr. K. Sugimoto (Chair: Dr. Y. Ishii)	**Symposium (6)** Regulatory aspects -from hazard identification to risk assessment- Dr. D. Kirkland Dr. S.M. Galloway Dr. J.T. MacGregor Dr. D. Blakey (Chair: Dr. T. Sofuni)
12:00	Registration	**Luncheon seminar** Sponsored by Amway Japan Limited Nutrilite Health Institute Dr. M. Fenech / Dr. M. Lemay (Chair: Dr. N. Tanaka)	**Closing Remarks**
13:00	**Opening Address**		
14:00	**Keynote lecture (1)** Dr. A.T. Natarajan (Chair: Dr. G. Obe)	**Poster Session**	
15:00	**Symposium (1)** Cytogenetic epidemiology Dr. S. Bonassi Dr. H. Norppa Dr. N. Nakamura (Chair: Dr. J. Tucker)	**Symposium (4)** Chromosome instability Dr. W.F. Morgan Dr. M. Honma Dr. A. Lyakhovich (Chair: Dr. M. Honma)	
16:00	Coffee break	Tea break	
17:00	**Symposium (2)** Children / clinical / germ cell Dr. T. Teh Dr. T. Nomura Dr. A. Fučić Dr. H. Tateno (Chair: Dr. I.D. Adler)	**Symposium (5)** Miscellaneous abnormality Dr. A. Inoue Dr. P.E. Bryant Dr. T. Ono Dr. R.V. Williams (Chair: Dr. M. Fenech)	
18:00	Hotel check-in		
19:00	**Welcome mixer**	**Banquet**	
20:00			
21:00			