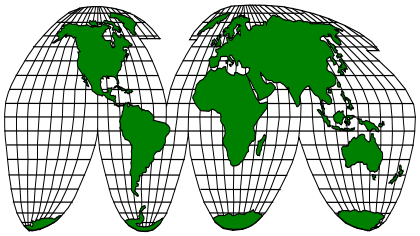


International Workshops on Genotoxicity Testing (IWGT)

Second Announcement

7TH INTERNATIONAL WORKSHOP ON GENOTOXICITY TESTING

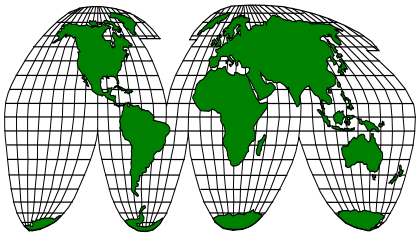
At the
National Cancer Center Research Institute
5-1-1 Tsukiji, Chuo-ku
Tokyo, 104-0045
Japan

http://www.ncc.go.jp/en/

On
8th-10th November 2017

Registration is now open:

http://www.iwgt2017.org/

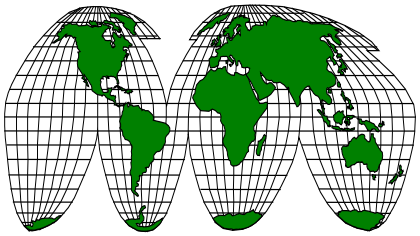


International Workshops on Genotoxicity Testing (IWGT)

7th International Workshop on Genotoxicity Testing

IWGT has held 6 previous workshops (Melbourne, 1993; Washington, 1999; Plymouth, 2002; San Francisco, 2005; Basel, 2009, Foz do Iguacu, Brazil, 2013). The consensus recommendations from these have been highly influential in shaping the revisions to OECD guidelines and the recommendations in the original and revised ICH S2 guidance. There are now new challenges facing the genetic toxicology community, new assays to consider, and new approaches to analysis of genotoxicity data.

IWGT will therefore hold its 7th workshop in Tokyo, Japan, as a satellite meeting immediately prior to the 2017 International Conference on Environmental Mutagens ICEM (http://www.icem2017.org/), which will be held in Seoul, Korea, and directly after the 46th Meeting of the Japanese Environmental Mutagen Society JEMS (http://www.jems2017.com/en/index.html), which will be held in Tokyo, Japan.



International Workshops on Genotoxicity Testing (IWGT)

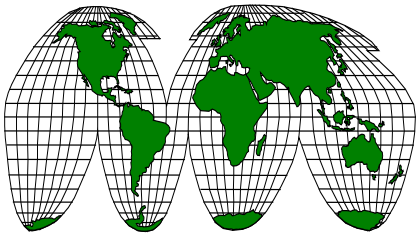
At the 7th IWGT, the following Working Groups will be formed:

1. A Working Group on the use of 3D models, led by Stefan Pfuhler, USA. The focus of the WG will be:

- Introduction to the concept of genetox testing in tissue models
- Status review of available genetox data generated in skin, liver and lung 3D tissue equivalents
- Validation status of the most developed 3D assays – the 3D skin micronucleus and comet assays
- Discuss test strategy fit and develop recommendations

2. A Working Group on emerging in vitro mammalian genotoxicity systems: endpoints and cell types, led by Bhaskar Gollapudi, USA. The group will critically assess emerging in vitro tools for measuring gene mutations in mammalian cell cultures, covering the following points:

- Basic algorithm for strategic placement of in vitro mutation assays
- Define basic principles of emerging assays
- Define current state of emerging assays
- Define research needs for the emerging assays to make them useful for regulatory applications
- In vitro models that can be used as surrogates for predicting in vivo response at the same locus
    - Higher throughput assays that are less laborious and less expensive
    - In vitro models to address mechanistic questions dealing with in vivo mutagenicity
- Focus groups will be:
    - Improving existing assays by applying new technologies
    - Mutation assays using cell lines from transgenic rodents
    - In vitro Pig-a mutation assays
    - Novel approaches to detect gene mutations in cell cultures



3. A Working Group will revisit the Salmonella mutagenicity (Ames) test, led by Rita Schoeny, USA, to discuss topics including these:

- Criteria for positive and negative responses; e.g. is there a place for alternatives to the 2x rule, such as Global Evaluation Factors or statistics?
- Criteria for acceptable assays and consideration of laboratory proficiency
- Consideration of the five most widely used strains as well as what can be learned from use of others. Consideration of a data-based approach to defining a minimum strain set.
- How can strains best be maintained?
- Status of in silico SAR tools for prediction of mutagenicity in the Ames test. Would predictions change if positivity criteria change?

4. A Working Group will discuss aspects of risk assessment of aneugens, led by Francesco Marchetti, Canada, covering:

- Molecular mechanisms of chromosome segregations and differences between somatic and germ cells
- Utility of the Adverse Outcome Pathway approach to elucidate the mechanisms of aneuploidy
- Role of aneuploidy in carcinogenesis: initiation, promotion, or progression?
- Secondary effects of aneuploidy and their involvement in adverse health outcomes
- Aneuploidy in germ cells and hereditary diseases
- Implication of aneuploidy for human risk assessment

5. A Working Group, led by David Kirkland, UK, will discuss in vivo strategies:

- Can in vitro test outcome (mutagen, clastogen, aneugen) be used to suggest the appropriate in vivo test?
- Possibility to choose a single test instead of 2 tests to follow-up on an in vitro positive?
    - What can we learn from the historical database of overlapping TGR & comet results?
    - Can the comet assay substitute for the TGR, and in what circumstances?
- Are the OECD guideline default tissues (liver + site of contact) for the in vivo comet assay sufficient to detect expected positives?
    - How many tissues need to be tested in the comet assay to be predictive of (a) genotoxicity, (b) carcinogenicity?
    - Is there a need to include glandular stomach as well as duodenum for site-of-contact in the comet assay with orally dosed substances?
- What is “adequate exposure” and the proper route of exposure (i.p. vs oral or inhalation) for bone marrow MN test acceptability?
    - Are certain tissues or routes of exposure preferable, particularly for the in vivo MN test?
    - Is the i.p. route considered preferable to the normal route of human exposure (oral, inhalation, dermal) because it minimizes first pass metabolism in the liver?
    - Is demonstration of exposure in the plasma sufficient to ensure exposure of the bone marrow in a micronucleus test?
    - What is considered “insufficient” bone marrow exposure that might lead to a requirement to perform a site-of-contact comet assay instead of a bone marrow MN test?
- Are diet and drinking water as effective as gavage dosing for all in vivo tests?
- What is the state of validation of the MN assay in alternative tissues (i.e. liver, G.I. tract)?
- Where does the Pig-a assay fit into regulatory in vivo testing?

6. Finally, a Plenary Symposium, led by Carole Yauk, Canada, will discuss the state-of-the-science, current application and added-value of high- dimensional data in genetic toxicology testing including:

- Single-molecule sequencing
- Adductomics
- Whole genome transcriptional profiling
- High-content phenotype-based assays