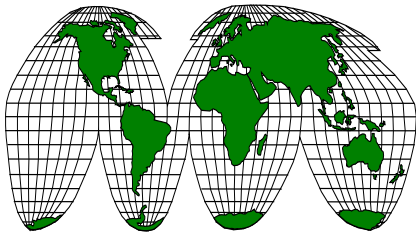


International Workshops on Genotoxicity Testing (IWGT)

First Announcement

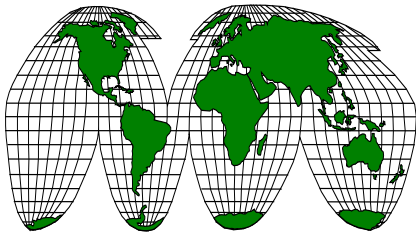
7TH INTERNATIONAL WORKSHOP ON GENOTOXICITY TESTING

National Cancer Center Japan
5-1-1 Tjukiji, Chuo-ku
Tokyo, 104-0045
Japan

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

8th-10th November 2017

Registration details coming soon



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 Iduacu, 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 as a satellite meeting immediately prior to the 2017 International Conference on Environmental Mutagens (ICEM), which will be held in Seoul, Korea, and directly after JEMS.

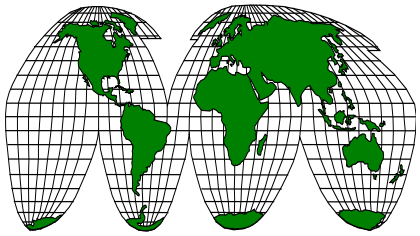
At the 7th IWGT, the following subgroups will be formed:

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

- Status review of the most developed 3D model based genotoxicity assays – the 3D skin micronucleus and comet assays.
- Discussion of genotox testing using other 3D models, e.g. lung and liver.
- Validation status of skin-based assays

2. **A subgroup 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



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- Focus groups will be:
  - In vitro Pig-a mutation assays
  - Mutation assays using cell lines from transgenic rodents
  - Improving existing assays by applying new technologies

3. A subgroup will revisit the Ames test, led by Rita Schoeny, USA, discussing:

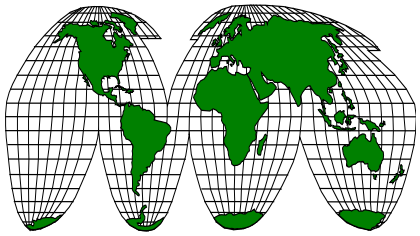
- Positivity critieria: is there a place for alternatives (e.g. GEF) to the 2x rule or statistics?
- Do we need all five strains (strain specific effects)?
- Status of in silico SAR tools for Ames prediction. Would predictions change if positivity criteria change?

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

- Utility of the Adverse Outcome Pathway approach to elucidate the mechanisms of aneuploidy
- Differences in the Spindle assembly checkpoint between somatic and germ cells and how they affect the response to aneugens
- Chromothripsis as a secondary effect of aneuploidy and its implication for adverse health outcomes
- Role of aneuploidy in carcinogenesis and its implications for human health risk assessment
- Sex-specific risk of aneuploidy

5. A subgroup, 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?



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- 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

IWGT Steering Committee:

Dr Roland Froetschl	BfArM, Germany
Dr Bhaskar Gollapudi	Exponent Consulting, USA
Dr Masa Honma (Co-Chair)	NIHS, Japan
Prof David Kirkland (Co-Chair)	Kirkland Consulting, UK
Dr Hans-Joerg Martus (Chair)	Novartis Institutes for Biomedical Research, Switzerland
Dr Rita Schoeny	EPA (retired), USA
Dr Yoshifumi Uno	Mitsubishi-Tanabe Pharma, Japan