終段階です　何故ポストラヘルを行なう必要があるのかわかった方は，ご連絡お待ちしています

シンポシウムの3項
　本シンポシウムにより遺伝毒性発がん物質に閾値を設定できる可能性が認識されたというのは遺伝毒性に閾値が在るのか，発がん性に閾値が在ると言っているのか不明です

　以上適当に議事録に取り入れてください

その他

　次回（第13回）は3月初旬～中旬を予定

添付資料一覧

| 資料番号 | 内容 |
|---|---|
| 1 | コウシ酸の遺伝毒性リスク評価の説明 |
| 2 | コウシ酸の遺伝毒性に関する新規データ |
| 3 | 海外コンサルタントからの提言 |
| 4 | 国際シンポシウムプログラム |

文責
森田　健

日本環境変異原学会臨時委員会

# 「食品および食品添加物等に関する遺伝毒性の検出・評価・解釈」

厚生労働科学研究費

# 「食品添加物等の遺伝毒性検出の戦略に関する研究」

## 第 13 回検討会議事録（案）

2004 年 3 月 15 日　14 00～17 00
インダストリアルホール 中会議室

参加者　長尾，祖父尼，田中，宇野，中嶋，林，森田，本間（議事録），佐々木
欠　席　葛西，布柴，太田，能美

1　前回の議事録確認

森田委員が作成した前回(鎌倉ミイーテング)議事録の内容に関しては了承された　また，鎌倉ミイーテング，東京シンポシウムで利用したすへての資料を添付資料として，追加する

- Dr Tweats より提出されるコンサルテーションレポートを最後の添付資料として添付する
- 添付資料が多いため，議事録に添付資料一覧を入れる

2　平成 15 年度報告書と次年度計画

- 本年度研究報告書の提出の締め切りは 4 月 10 日で，とりまとめは林委員長，本間委員が行う
- 各試験分担者からの分担報告書はすべて提出済み　経理報告書も予定通り提出・処理されている
- 次年度もほぼ今年度と同し規模の予算で申請しており，近いうちに提出か求められる交付申請書には，今年度の具体的な計画を作文し提出する
- 来年度の研究班には森田委員か分担研究者として参画し，データのとりまとめ等を担当するように現在調整中
- 来年度は，コンサルテーションミイーテイングを予定していないので，具体的な試験を中心に行う予定

3　2004 年 2 月の鎌倉，東京会議について

- 中嶋委員より会議に関する経理報告，および財団に提出する経理報告書の内容についての説明があった
- 今回の会議の成果については，Dr Tweats より提出される報告書の内容か重要であり，報告書を検討した上で今後の方向性を検討する
- 会議ではコウン酸の発がん性，特に肝臓に対する発かん性に疑問か集中した　コウシ酸に遺伝毒性であったとしても甲状腺がんとの直接作用の関係はないであろう　また，肝がんを引き起こすとしても，それが遺伝毒性によるものがはっきりしない　従って，肝臓に対する遺伝毒性の有無を明らかに必要があるのではないか？
- 肝臓での小核試験を実施する際の問題点（ラノト or マウス，加齢による影響，肝部分切除の影響）が話し合われた
- 次年度コウシ酸に関する試験としては以下の 4 試験を追加試験として行うことか提案された □肝小核，□肝臓での DNA アダクトの検出，□光毒性を考慮した MLA，

□ラット肝 UDS，□TK 試験

- 試験データの信頼性を向上させるため，GLP での試験，もしくは試験プロトコール等の精査の必要性である
- 今年度でコウン酸に関する試験を終了させ，試験結果については来年度中に論文にまとめることを目指す
- 次回のモデル化合物としてはアマランス，もしくは他のアゾ化合物を候補とする化合物か決まり次第，手分けしてこれまでの試験データをレヒューする
- 具体的な進め方に関しては，Dr Tweats の報告書を精査した上で，もう一度話し合う

4　その他

次回検討会は 4 月 22 日(木)　午後 2 時よりインダストリアルホール

文責
本間　正充

# Risk Assessment of Kojic Acid Which Has Been Used as a Food Additive

JEMS Ad hoc Committee

## History of Regulation of Food Additives in Japan

1880's Establishment of regulation laws for foods and drinks
1947 The Food Sanitation Law(Ministry of Health and Welfare)
1955 Revision of the Law (Arsenite contamination in powdered milk)
1960 The Japanese Standards for Food Additives 1st ed
1974 Use of AF-2 was banned
1996 Revision of the Law (JECFA, OECD, FDA)
Evaluation of Existing Food Additives (125)
2003 Cabinet Office Food Safety Commission
Risk Evaluation, Risk Communication

## Regulatory Law for Food Additives in Japan

General toxicity, Reproduction, Teratogenicity, Carcinogenicity, Genotoxicity →ADI

Substances that induced tumors and showed *in vivo* genotoxicity cannot be used as food additives There are no safe doses for such substances

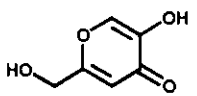
**JECFA (FAO/WHO)**

There is a single copy of DNA in every cell, therefore, it is reasoned, there can be no threshold of damage below which DNA damage has no consequence, hence, there can be no safe exposure level to a carcinogen that is genotoxic

## Food Additives in Japan

| | |
|---|---|
| Designated additives | 338 |
| Existing additives (Natural) | 489 |
| Natural flavor | 612 |
| Others | 72 |

Kojic acid
- Existing additive (No standards for compositions or usage)
- Prevention of enzymatic browning、Antibiotics
- Produced by *Aspergillus*(crystallized from culture medium)




Kojic acid M W 143 118

16/10/2003

Use of KA as a food additive was banned

① KA induced hepatomas and its genotoxicity was suggested

② KA is intentionally added to foods.

③ KA is not used at present in any countries

KA will be deleted from the Existing Food Additive List in near future

- KA might be a useful example

for establishment of strategy to identify genotoxicity

for re-evaluation of general rules for risk assessment of genotoxic carcinogens.

- KA is used in cosmetics (cream)

It is under moratorium status



## Carcinogenicity of KA in Mice

(Dec 2002 Consultation committee for drugs and foods, MHLW)

| | KA in diet (%) | No B6C3F1 | Tumor incidence (%) | |
|---|---|---|---|---|
| | | | Thyroid adenoma | Hepatoma |
| M | 0 | 48 | 2 | 48 |
| | 1 5 | 52 | 65* | 69 |
| | 3 | 53 | 87* | 47 |
| F | 0 | 52 | 2 | 0 |
| | 1 5 | 51 | 8 | 4 |
| | 3 | 49 | 80* | 10* |

*; P<0 05

(Fujimoto et al , 1998)

## Genotoxicities of KA in Bacteria

(Dec 2002 Consultation committee for drugs and foods, MHLW)

| DNA damage | Cells | S9 | Assay No | Result |
|---|---|---|---|---|
| SOS repair | *E coli* | +,- | 1 | - |
| Rec assay | *B subtilis* | - | 1 | + |
| Gene mutation | *S typhimurium* TA100, TA98, Others | +,- | 7 | + 5, - 2 |

## Genotoxicities of KA in Mammalian Cells *in Vitro*

*(Dec 2002 Consultation committee for drugs and foods, MHLW)*

| Cell | Marker | S9 mix | No Exp | Max conc. (mg/ml) |
|---|---|---|---|---|
| V79 | *Hprt* mutation | +,- | 1 | - (3)* |
| L5178Y | *Hprt* mutation | +,- | 1 | - (1 4)* |
| CHO-K1 | SCE | +,- | 1 | + |
| CHO-K1 | CA | +,- | 1 | + |
| CHL/IU | CA | +,- | 2 | +, - (2) |
| HepG2 | MN | +,- | 1 | - (8)* |
| SVK14 | MN | +,- | 1 | - (8)* |

## Genotoxicities of KA *in Vivo*

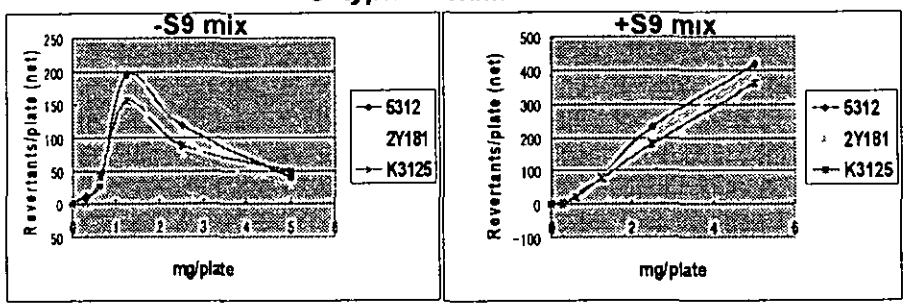
*(Dec 2002 Consultation committee for drugs and foods, MHLW)*

| | Tissue, cell | Damage | Max dose g/kg/day | No Exp | Results |
|---|---|---|---|---|---|
| Mice | BM | MN | 1g x2 | 3 | - |
| | Hepatocyte (PH) | MN | 1g x1 | 1 | + |
| | Hepatocyte | Comet | 1g x1 | 2 | +,- |
| | | | 3% in diet, 4 days | 1 | + |
| | Liver | LacZ | 1 6g x28 | 1 | - * |
| | Thyroid | Comet | 0 75g x1 | 1 | - |
| Rats | BM | MN | 2g x2 | 1 | + |
| | PB | MN | 2g x1 | 2 | + |
| | Hepatocyte | MN | 2gx1 | 2 | - |
| | Hepatocyte | Comet | 1g x1 | 1 | + |
| | Hepatocyte | UDS | 1 5g x 1 | 1 | - * |



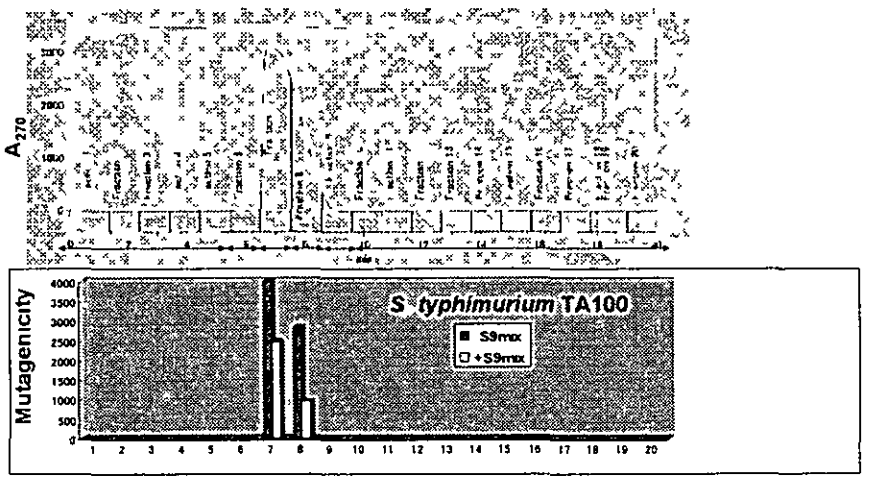
## Mutagenicity Test on Three Lots of Kojic Acid

*S typhimurium* TA100

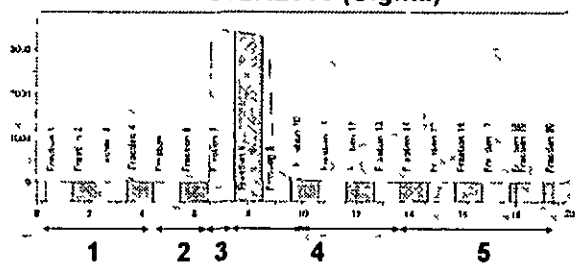



| | | |
|---|---|---|
| 5312 | 124 revertants/mg | 73 revertants/mg |
| 2Y181 | 157 | 77 |
| K3125 | 122 | 83 |

## Is Kojic Acid Mutagenic?



052K2516 (Sigma)




| Solvent DMSO | Mutagenicity (revertants/mg) -S9mix | +S9mix |
|---|---|---|
| Original | 89 | 41 |
| Fraction 1 | 0 | 0 |
| 2 | 0 | 0 |
| 3 | 95 | 44 |
| 4 | 83 | 45 |
| 5 | 0 | 0 |

## Genotoxicity of KA in Human Lymphoblatoid cells *in Vitro*

| Marker | Cell | | Conc KA (mg/ml) |
|---|---|---|---|
| Mutation (TK) | TK6 | + | 3~4 |
| | WTK-1 | + | 2~4 |
| DNA damage (Comet) | TK6 | + | 2 5~5 |
| | WTK-1 | + | 2 5~5 |
| Chromosome Ab (MN) | TK6 | + | 2~3 |
| | WKT-1 | + | 1~2 |

## Genotoxicity of KA in Mammals *in Vivo*

**C3B6 F1, female, liver**

| | |
|---|---|
| Mutation *LacZ* | 3% in diet 4 weeks |

**Negative**

## Detection of KA in Fermented Foods

(Dec 2002 Consultation committee for drugs and foods, MHLW)

Positives/Examined

- Miso 2/15 1 ppm at maximum
- Shoyu 1/5 1 ppm at maximum
- Sake 0/9
- A orizae 19/47 → Koji 175ppm (1)
  3 (3)
  1 6 (3)
  < 0 1 (12)

Human exposure to KA was estimated to be 0 6 μg/kg/day by assuming daily Miso intake being 3 g and Shoyu 27 ml /day

## HERP Index (Ames-Gold)

$TD_{50}$ =1 4x10$^4$ mg/kg/day
(KA in diet 3%, cancer incidence 10%)

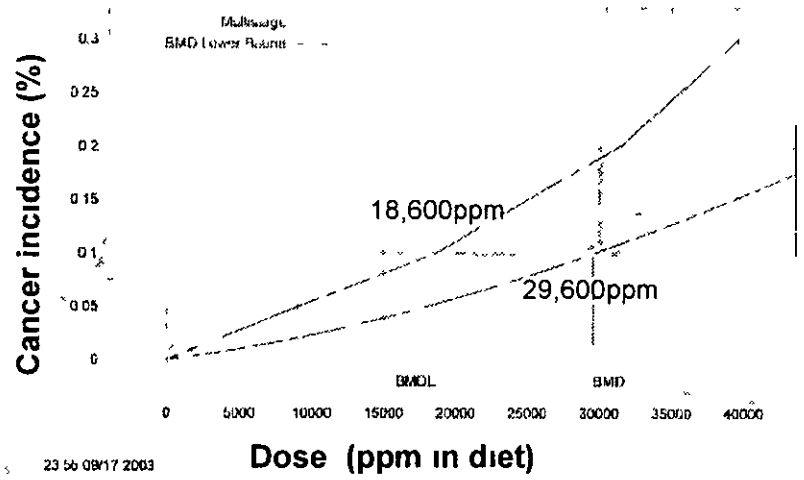
Human exposure =0 6 μg/kg/day

HERP=4 2x10$^{-8}$

**HERP of Foods**

| | |
|---|---|
| Wine (EtOH) | 5x10$^{-2}$ |
| Lettuce (Caffeic acid) | 3x10$^{-3}$ |
| PhIP | 8x10$^{-6}$ |
| PCNB | 4x10$^{-9}$ ← KA |

## Multistage Model with 0.95 Confidence Level






B6C3F1 Female Mice

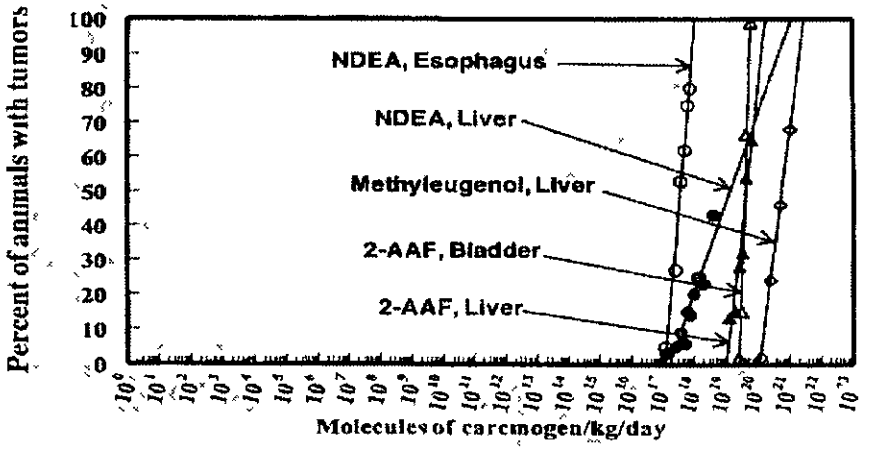
$LED_{10}$ 18,600 ppm KA in diet
KA intake at $LED_{10}$ = 2.4x10$^6$ μg/kg/day
KA intake at $LED_{100}$ = 2 4x10$^7$ μg/kg/day

Human
Exposure = 0.6 μg/kg/day

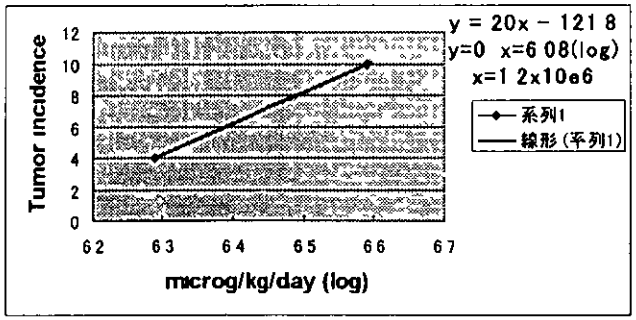
Cancer Risk
0 6/2 4x10$^{-7}$x1/(0 025/50)$^{0\ 25}$ = 1.65x10$^{-7}$

## Thresholds of Various Genotoxic Carcinogens

by Waddell, 2003



## Threshold for Carcinogenicity and Human Exposure




| | |
|---|---|
| Threshold in mice | 1.2 x$10^6$ μg/kg/day |
| Application to human | 1.8 x$10^5$ μg/kg/day |
| Human exposure | 0.6 μg/kg/day |

HERT=3 3x$10^{-6}$

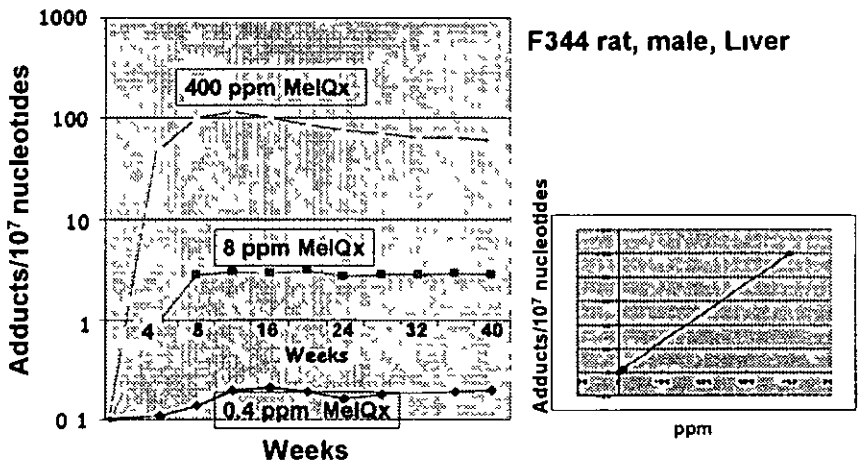
## Risk of KA to Cancer Development

Assessment based on the mouse hepatoma

| | |
|---|---|
| HERP | 4.2x$10^{-8}$ |
| $LED_{10}$ | 1.65x$10^{-7}$ |
| HERT | 1.1x$10^{-6}$ |



## Dose Effects of MeIQx on DNA Adduct Levels




F344 rat, male, Liver

Hirose M, 1995

## Dose Effect of MeIQx on DNA Adduct Levels

$^{32}$P-post labeling method

16 μg/kg/day~16 mg/kg/day

4, 8,16, 24, 32, 40 wk, diet

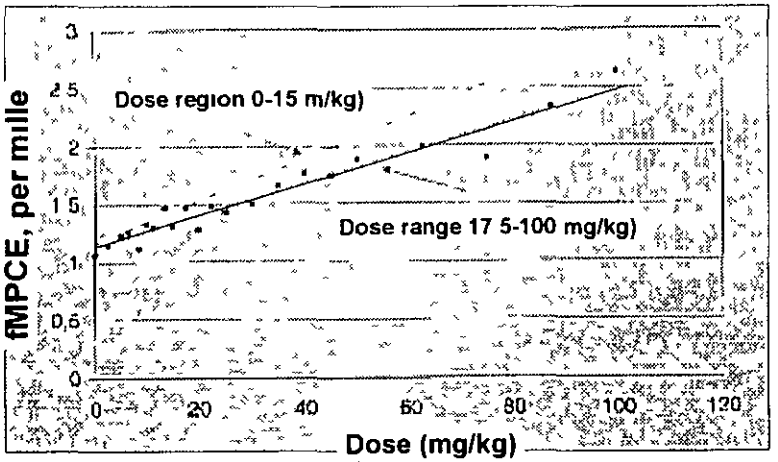
AMS by Turteltaub et al , 1995

0 058 ~34 μg/kg/day

24h (gavage), 1 wk, 6 wk (diet)

Linear dose effects were observed

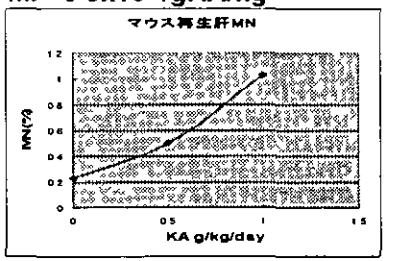
## Low Dose Effect of Acrylamide on MN Induction in Mouse Bone Marrow



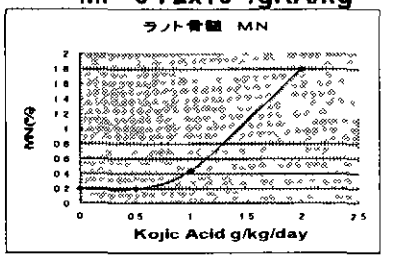

Abramsson-Zetterberg L, 2003

## Risk of KA to DNA Damages in Human

MN (Mouse regenerating liver)
MF=0 8x10$^{-2}$/gKA/kg




MN (Rat bone marrow)
MF=0 72x10$^{-2}$/gKA/kg




Human exposure 0 6μg/kg/day
Cell number in human body 6x10$^{13}$
10% of these cells can be expected to proliferate

Risk of KA to MN induction 1 8 x10$^{6}$ /human
Background MN level 1 2 x10$^{10}$/human

Is the load of 10$^{-4}$ genetic damages of the background can be acceptable?

# *Report on the Kamakura Consultation Meeting*

David Kirkland

## *Consultation Exercise*

- Re-evaluation by MHLW of selected compounds induced need for new strategy
- Used Kojic acid as an example Carcinogenicity & genotoxicity data sets are complex We asked
  - which tests provided useful information?
  - which tests did not provide useful information?
  - can any quantitative assessment (e g potency) be made from any studies? If so which?
  - Is Kojic acid a free radical scavenger?

## Genotoxicities of KA in Bacteria

Dec 2002 Consultation committee for drugs and foods MHLW

| DNA damage | Cells | S9 | Assay No | Result |
|---|---|---|---|---|
| SOS repair | *E coli* | +,- | 1 | - |
| Rec assay | *B.subtilis* | - | 1 | + |
| Gene mutation | *S typhimurium* TA100, TA98, Others | +,- | 7 | + 5, - 2* |

## Genotoxicities of KA Mammalian Cells *in Vitro*

Dec 2002 Consultation committee for drugs and foods MHLW

| Cell | Marker | S9 mix | No Exp | Max conc (mg/ml) |
|---|---|---|---|---|
| V79 | *Hprt* mutation | +,- | 1 | - (3)* |
| L5178Y | *Hprt* mutation | +,- | 1 | - (1 4)* |
| CHO-K1 | SCE | +,- | 1 | + |
| CHO-K1 | CA | +,- | 1 | + |
| CHL/IU | CA | +,- | 2 | +, - (2) |
| HepG2 | MN | +,- | 1 | - (8)* |
| SVK14 | MN | +,- | 1 | - (8) |

## Genotoxicities of KA *in Vivo*

Dec 2002 Consultation committee for drugs and foods MHLW

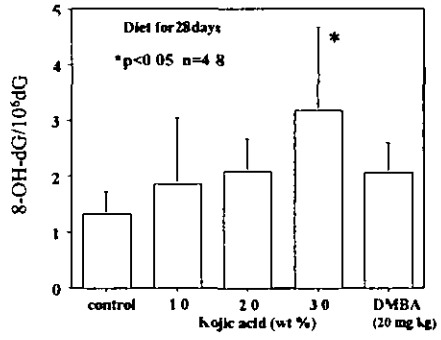
| | Tissue cell | Damage | Max dose g/kg/day | No Exp | Results |
|---|---|---|---|---|---|
| Mice | BM | MN | 1g x2 | 3 | - |
| | Hepatocyte (PH) | MN | 1g x1 | 1 | + |
| | Hepatocyte | Comet | 1g x1 | 2 | + |
| | | | 3% in diet, 4 days | 1 | + |
| | Liver | LacZ | 1 6g x28 | 1 | * |
| | Thyroid | Comet | 0 75g x1 | 1 | - |
| Rats | BM | MN | 2g x2 | 1 | + |
| | PB | MN | 2g x1 | 2 | + |
| | Hepatocyte | MN | 2gx1 | 2 | - |
| | Hepatocyte | Comet | 1g x1 | 1 | + |
| | Hepatocyte | UDS | 1 5g x 1 | 1 | -* |

Summary of assay results

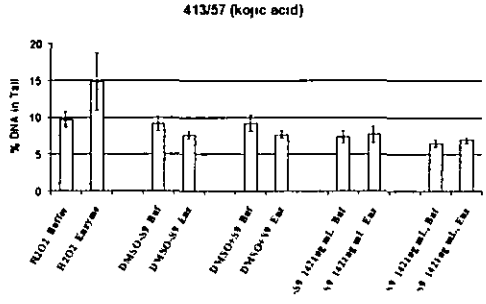
1 Osmolarity and pH of Fagle MEM in addition with kojic acid
No effect on in vitro testing results
2 Bacterial reverse mutation assay with purified fractions of kojic acid by HPLC
Kojic acid itself is mutagenic and no mutagenic compounds were contaminated
3 Bacterial reverse mutation assay reevaluation, mutation spectrum under black light
A T to C G and G C to C G transversions were observed
No effect on testing results by UVA
4 Photo plasmid relaxation assay
Positive Super oxide radical and $H_2O_2$ production were indicated
5 In vitro genotoxicity assay with TK6 and WTK 1 cells Positive
6 In vitro Comet assay with TK6 and WTK 1 cells Positive
7 In vitro photo-genotoxic assay with Tk6 cells Positive
8 Drosophila DNA repair and wing spot assay Negative
9 In vivo genotoxicity assay in the liver of female Muta mice Negative
10 8-OH-dG analysis in the liver of female Muta mice Positive
11 Cell proliferation analysis in the liver of male F344 rats
Positive continuous RDS induction was observed in the feeding study

10 8 OH-dG analysis in the liver of female Muta mice

**Effect of kojic acid on the 8 OH-dG levels in mouse liver DNA**




## *FPG Comet Assay with KA in CHO Cells*




## *Concern and Recommendations*

- Genotoxicity results variable, particularly in mammalian cells, but majority of bacterial assays *positive*
  - unsure of sensitivity/specificity of plasmid DNA relaxation assay
- No consistent mechanism of *in vitro* genotoxicity
  - some photo genotoxicity assays suggest active oxygen but negative in TA102
- Investigate free radical/ active oxygen mechanisms *and look for adducts in vitro*

## *Genotox Concerns and Recommendations (2)*

- Hepatocyte MN positive in mice (with partial hepatectomy) but not in young rats
- Bone marrow MN positive in young rats but not mice
- May not be due to species differences as much as different metabolism in young rats
- Repeat bone marrow MN test in adult rats
- Perform metabolism studies to check species differences

## *Genotoxicity Results (2)*

- *In vivo* hepatocyte comet assays positive in rats and mice
  - seem to have particular significance regarding carcinogenicity
- Comet assay measured tail length, not tail moment
- Could be same amount of DNA but smaller fragments
- Rescore slides to measure tail moment

## Carcinogenicity of KA in Mice

**Dec 2002 Consultation committee for drugs and foods MHLW**

| | KA in diet (%) | No B6C3F1 | Tumor incidence (%) | |
|---|---|---|---|---|
| | | | Thyroid adenoma | Hepatoma |
| M | 0 | 48 | 2 | 48 |
| | 1 5 | 52 | 65* | 69 |
| | 3 | 53 | 87* | 47 |
| F | 0 | 52 | 2 | 0 |
| | 1 5 | 51 | 8 | 4 |
| | 3 | 49 | 80* | 10* |

P<0 05 (Fujimoto et al 1998)

## *Thyroid Tumours and Kojic Acid*

- Papillary adenomas induced
- No increase in malignant tumours
- Inhibition of iodine uptake – decrease in serum T3/T4 levels—compensatory increase in TSH release by the pituitary—thyroid cell proliferation
- Classical mechanism for thyrotropic substances
  - lower doses cause no hormonal disruption and no histological changes in thyroid histopathology
  - effect of KA on thyroid was reversible

## *Liver Tumours and Kojic Acid (2)*

- Liver tumours in mice – unsure if malignant? 'Hepatomas in untreated males very high (48) if hepatocellular carcinomas – important to know
  - Rescore slides and define if malignant or benign tumours
- Quality of test material produced from Aspergillus re mycotoxins - 3% of diet, so small amounts of potent contaminants could be important in long-term studies
  - Are there analysis data on content of mycotoxins and other contaminants?
  - Not explain mouse tumours but rat GST-P positive foci?

## *Recommendations*

- Induction of RDS in feeding study in rat
  - Test to see if this also happens in mouse
- Suggest non-genotoxic mechanism? Threshold?
  - Negative MutaMouse studies also
- Need to generate adduct data in mice (and rats?)
- Need new p53 tumour study (previous group sizes too small and high level animal infection)
- Exposure and ADME data (at high doses) critical to understanding inconsistent results
- Need new lifetime rat carc study

## *Recommendations*

- Also lack data in full rat carc study
  - conduct new study using KA with no mycotoxins
- Tumours likely because of thyroid stimulation
  - Literature review of thyroid/liver connection would help
- However lack of adducts, and negative mouse p53 study, may allow conclusion that carcinogenicity is due to non-genotoxic mechanism and not linked to genotoxicity

## Regulatory Law for Food Additives in Japan

**General toxicity, Reproduction, Teratogenicity, Carcinogenicity, Genotoxicity →ADI**

**Substances that induced tumors and showed *in vivo* genotoxicity cannot be used as food additives There are no safe doses for such substances**

**JECFA (FAO/WHO)**

**There is a single copy of DNA in every cell therefore it is reasoned there can be no threshold of damage below which DNA damage has no consequence hence there can be no safe exposure level to a carcinogen that is genotoxic**

## *Lack of Relevance for Humans*

- Are there conditions where genotoxicity will not be appropriate to human exposure e g where genotoxicity results from changes in physiology, non-DNA target, lack of detoxification etc?
- What evidence is needed to establish thresholds
- Consultants to look at data/tests/endpoints
- Recommend tests that are most reliable
- Advice needed on the weight to give specific data, potency etc

## *Threshold or Non-Relevant Mechanisms*

- Interaction with non-DNA targets
- DNA-reactive chemicals/metabolites at high concentrations, but which, at low concentrations are effectively conjugated and unable to form adducts
- Intermediates formed under specific metabolic conditions *in vitro* that will not be formed in rodents *in vivo* or in humans
- Threshold dose = Lowest Observed Effect Level

## *UK Food Standards Agency*

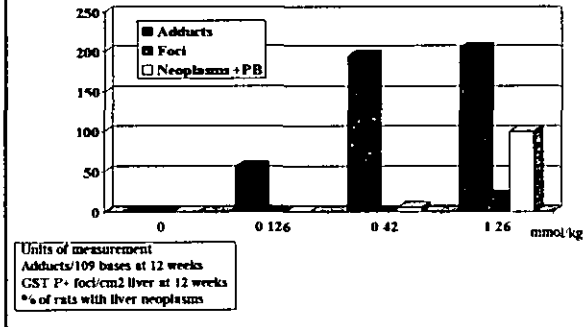
- Dr Benford will describe in more detail
- Not all positive results have same significance
  - Rapid and extensive detoxification can allow a positive *in vivo* mutagen to be regarded as having a threshold (route important)
  - Examples of compounds with *in vitro* genotox that induce tumours where the tumours are clearly due to a non-genotox mechanism e g finastende, benzyl acetate etc
- Mechanistic information is vital

## *Indirect Mechanisms of Genotoxicity (Scott et al, 1991)*

- Enzyme induction
- Imbalance of DNA precursors
- Energy depletion
- Production of active oxygen species
- Lipid peroxidation
- Sulphydryl depletion
- Nuclease release from lysosomes
- Inhibition of protein synthesis
- Protein denaturation
- Ionic imbalance
- High osmolality
- Low pH

* High cytotoxicity was not identified at this time

## *AAF Adducts & Tumours (Williams et al, 2000)*




## *How To Manage Food Mutagens*

- QSAR good first step in prioritising potential food mutagens for evaluation
- Unavoidable mutagens should be reduced to as low as reasonably practicable
- Correlations of potency between genotox data and carcinogenic potency difficult, but potent, multitest positives tend to be potent carcinogens Some examples of weak genotoxins being potent carcinogens

## *Threshold of Toxicologic Concern (TTC)*

- Possible to agree a (low) acceptable limit (not zero) for *unavoidable genotoxic carcinogens in foods*
  - low additional cancer risk exists (e g 1 new case per $10^6$ people exposed for a life time) Risk calculations done using most conservative (worse case) estimate of cancer risk from animal studies
- When limited (or poor quality) data, a daily intake level without appreciable concern cannot be calculated
  - Could use concept of Threshold of Toxicologic Concern (TTC) to set interim levels until better data available
- Use the TTC approach for unavoidable genotoxins to give targets for control levels

### *How To Define Threshold/Non-Relevant*

- Need to understand mechanism first before searching for threshold?
- Profile of results across test battery may suggest thresholded or non-relevant mechanism e g positive in 1, or perhaps 2, tests only
- Ames test positive compounds tend to be given more weight and are difficult to over-rule
  - May be able to over-rule mammalian cell positives where there are more non-relevant mechanisms giving positive results

### *Evidence of Threshold/Non-Relevant Mechanism*

- Good quality data are needed to be convinced that threshold or non-relevant mechanism exists
  - May need large experiments and need statistical advice on power and sensitivity of design
- Cannot rely entirely on shape of dose response curve, need to have mechanistic data
- Follow up testing of *in vitro* positives needs two *in vivo* tests
  - If negative *in vivo* need explanation why *in vivo* and *in vitro* are different
  - Need to carefully justify choice of *in vivo* test re endpoint seen as positive *in vitro*

### *Take Home Messages (from Kojic Acid)*

- Information used to make decisions on safety
- Information is taken from test data
- Not all tests provide useful information
- Adding more tests (data) does not necessarily increase the useful information
- Need to carefully select any additional tests to ensure they will add to useful information
- MORE = LESS

—International Symposium—

"Risk Assessment Strategy in Genotoxicity of Food and Related Substances"

JEMS

# 国際シンポジウム
## —食品関連物質等のリスクアセスメント戦略—

## 『遺伝毒性に閾値はあるか？！』

# PROGRAM/ABSTRACTS
# プログラム・要旨集

日時：2004年2月14日（土）9:30～17:30

会場：国際研究交流会館　3階国際会議場
（東京都中央区築地5-1-1 国立がんセンター構内）

厚生労働科学研究費（食品安全確保研究事業）
日本環境変異原学会（評価・解釈ストラテジ臨時委員会）
日本食品化学研究振興財団後援

# －International Symposium－
# "Risk Assessment Strategy in Genotoxicity of Food and Related Substances"

## 国際シンポジウム

## ―食品関連物質等のリスクアセスメント戦略―

## 『遺伝毒性に閾値はあるか？！』

**PROGRAM/ABSTRACTS**
プログラム・要旨集

日時　２００４年2月１４日（土）９　３０～１７　３０
会場　国際研究交流会館　３階国際会議場
（東京都中央区築地 5-1-1 国立がんセンター構内）

厚生労働科学研究費（食品安全確保研究事業）
日本環境変異原学会（評価・解釈ストラテジー臨時委員会）
日本食品化学研究振興財団後援

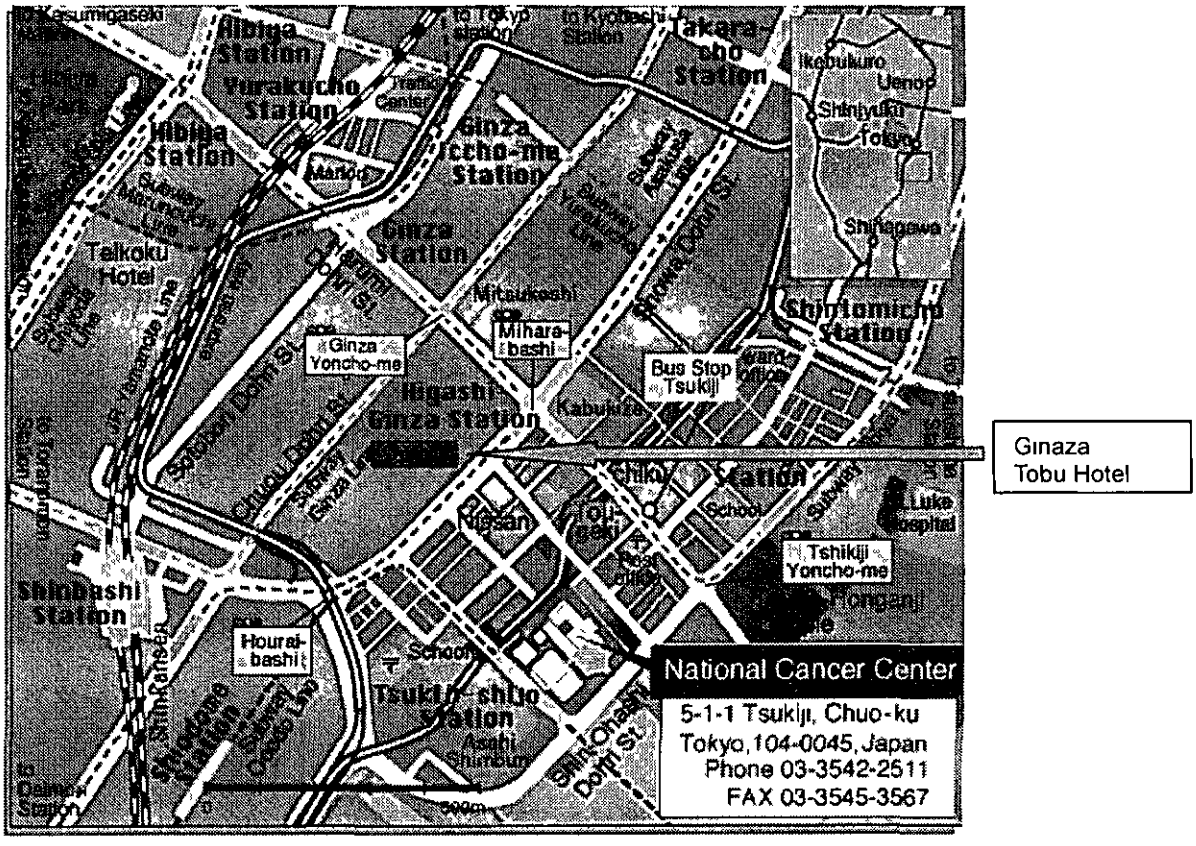
国際シンポシウム「食品関連物質等のリスクアセスメント戦略」
組　織　委　員　会

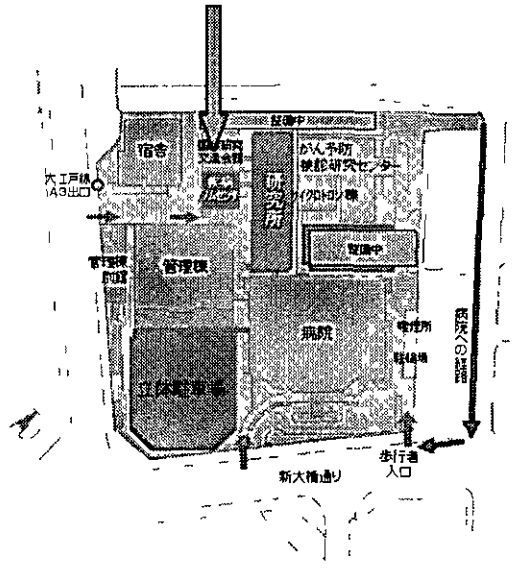
本シンポシウムの組織委員会は、日本環境変異原学会臨時委員会「食品および食品添加物等に関する遺伝毒性の検出・評価・解釈」と厚生労働科学研究班「既存添加物等における遺伝毒性評価のための戦略構築に関する研究」の合同メンバーによって構成されている。

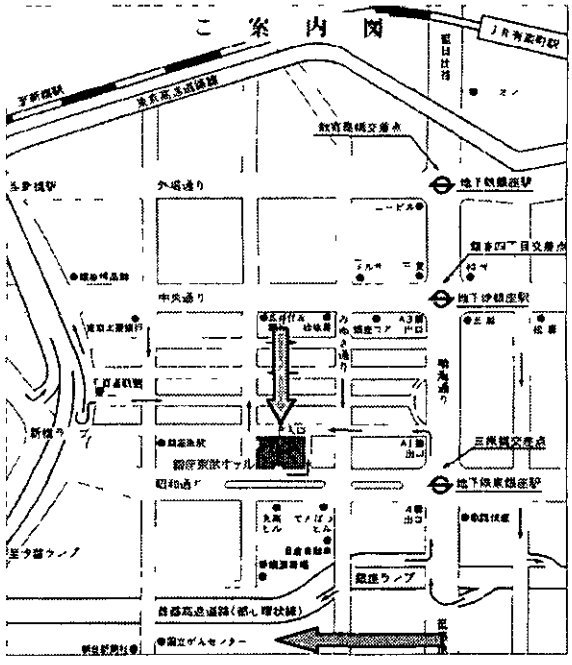
委員長　林　真（国立医薬品食品衛生研究所・変異遺伝部）
副委員長　長尾　美奈子（共立薬科大学）
委　員　宇野　芳文（三菱ウェルファーマ（株）・安全性研究所）
太田　敏博（東京薬科大学・生命科学部）
葛西　宏（産業医科大学・産業生態科学研究所）
佐々木　有（八戸工業高等専門学校・物質工学科）
祖父尼　俊雄（(株) ノバスシーン）
田中　憲穂（(財) 食品薬品安全センター・秦野研究所）
中島　圓（(財) 食品農医薬品安全性評価センター・遺伝毒性グループ）
布柴　達男（東北大学大学院・生命科学研究科）
能美　健彦（国立医薬品食品衛生研究所・変異遺伝部）
本間　正充（国立医薬品食品衛生研究所・変異遺伝部）
森田　健（国立医薬品食品衛生研究所・安全情報部）

【会場案内】

## Maps of National Cancer Center and Ginza Tobu Hotel



国際シンポシウム
—食品関連物質等のリスクアセスメント戦略—

『プログラム』

9 30-9 35　開会の挨拶　長尾　美奈子（共立薬科大学）

座長　宇野　芳文（三菱ウェルファーマ（株））

9 35-10 05　食品および食品関連物質の遺伝毒性試験データに基つく安全性評価の戦略
林　真（国立医薬品食品衛生研究所・変異遺伝部）

10 05-10 35　コンサルテーションミーティングの内容の紹介
David Kirkland（Scientific and Regulatory Consulting, Covance Laboratories Ltd , Harrogate, UK）

10 35-10 55　（休憩）

座長　本間　正充（国立医薬品食品衛生研究所）

10 55-11 25　In Vitro 染色体異常試験におけるデータ解釈の限界　核内倍加および毒性に依存する陽性反応に対する疑問
Sheila M Galloway （Merck Research Laboratories, West Point, USA）

11 25-11 55　In vivo において肝細胞に形成される巨大 DNA 付加体に対するコメット試験と不定期 DNA 合成試験の検出能力の比較　In vitro アフィティコリン処理による感度の向上
Veronique Thybaud（Genetic Toxicology, France, Aventis Pharma, Paris Research Center, Drug Safety Evaluation, France）

11 55-13 20　（昼食）

座長　田中　憲穂（(財）食品薬品安全センター秦野研究所）

13 20-13-50　食品と化粧品中の遺伝毒性物質の評価と解釈のための新技術
Marilyn J Aardema（The Procter & Gamble Co, Miami Valley Laboratories, USA）

13 50-14 20　トキシコゲノミクス　遺伝毒性における新機軸
David Blakey (Environmental Health Science, Safe Environments Programme, Health Canada, Canada）