12h30	**10**	**Conclusion and next steps (30min)**
		Following the discussion, the meeting will be invited to agree on next steps.
13h00	**11**	**Any other business (30min)**
13h30		*Meeting adjourns*

ICCA-LRI Workshop

Twenty-First Century Approaches to Toxicity Testing, Biomonitoring, and Risk Assessment
June 16 and 17, 2008
Renaissance Amsterdam Hotel, The Netherlands
FINAL Agenda

Workshop Chair
Richard Phillips, ExxonMobil

AGENDA AT A GLANCE

Monday, June 16, 2008

07.00 – 08.00	Registration and Continental Breakfast
08.00 – 09.00	Welcome and Workshop Objectives
09.00 – 10.00	Plenary Session I: The Context
10.00 – 10.30	Morning Break
10.30 – 12.30	Plenary Session II: Setting the Stage for the Parallel Symposia
12.30 – 14.00	Lunch
14.00 – 17.00	Three Parallel Symposium Sessions (including a 30 minute Afternoon Break)
17.00 – 18.00	Break / Aperitif
18.00 – 19.00	Reception and Poster Viewing
19.00 – 21.00	Group Dinner

Tuesday, June 17, 2008

07.00 – 08.00	Continental Breakfast
08.00 – 10.00	Three Parallel Symposium Sessions/Panel Discussions
10.00 – 10.30	Morning Break
10.30 – 12.30	Parallel Symposia Report Back
12.30 – 14.00	Lunch
14.00 – 15.30	Plenary Session III: Looking Ahead
15.30 – 16.00	Afternoon Break

DETAILED AGENDA

Monday, June 16, 2008

07.00 – 08.00	**Registration and Continental Breakfast**
08.00 – 08.50	*Session Chair:* **Richard Phillips**, ExxonMobil, Belgium Welcome • **David Duncan**, Unilever, UK, on behalf of the Cefic Research & Innovation Programme Council • **Antonio Lacerda de Queiroz**, European Commission, Belgium
08.50 – 09.00	Workshop objectives and expectation of outcome • **Richard Phillips**, ExxonMobil, Belgium

Plenary Session I: The Context

09.00 – 10.00	*Session Chair:* **Marc Willuhn**, Cefic (European Chemical Industry Council), Belgium *Speakers:* (30 minutes each, including Q&A) Dealing sensibly with environmental health risks in the 21st century • **Erik Lebret**, The National Institute for Public Health and the Environment (RIVM), The Netherlands Toxicity testing in the 21st century: A vision and a strategy • **Daniel Krewski**, University of Ottawa, Canada
10.00 – 10.30	**Morning Break**

Plenary Session II: Setting the Stage for the Parallel Symposia

10.30 – 12.30	*Session Chair:* **Tina Bahadori**, American Chemistry Council, USA *Speakers:* (30 minutes each, including Q&A) Public health opportunities of human biomonitoring within an evolving risk framework • **Gary Ginsberg**, Connecticut Department of Health, USA Omics-based biomarkers for chemical safety: An overview of EU efforts • **Jos Kleinjans**, University of Maastricht, The Netherlands ToxCast™: One step in fulfilling the NRC's vision of toxicity testing in the 21st century • **Robert Kavlock**, Environmental Protection Agency, USA Heavy metal and tobacco smoke toxicity and individual genetic susceptibility • **Karl Ernst von Muehlendahl**, Children's Hospital in Osnabrück, Germany
12.30 – 14.00	**Lunch**

Parallel Symposium Sessions

14.00 – 17.00

(including a 30 min **Afternoon Break**)

Session 1: Human Biomonitoring

Chair: **Ulrike Zimmer**, VCI (German chemical industry association), Germany
Rapporteur: **Herman Autrup**, University of Aarhus, Denmark
Recorder: **Ami Parekh**, ICF International, USA

Description of parallel symposia and charge to participants (15 minutes)
- **Ulrike Zimmer**, VCI (German chemical industry association), Germany

Speakers: (15 minutes each for the first two, 30 minutes each for the second two, with 45 minutes for discussion and Q&A)

The concept and results of the German health interview and examination survey for children and adolescents (KiGGS)
- **Bärbel-Maria Kurth**, Robert Koch Institute, Germany

The German environmental survey on children: Exposure of children to environmental factors
- **Marike Kolossa-Gehring**, Federal Environment Agency, Germany

Temporal trends in general population-based exposures
- **Dana Barr**, Centers for Disease Control and Prevention, USA

The German Human Biomonitoring Commission
- **Juergen Angerer**, University of Erlangen-Nuremberg, Germany

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14.00 – 17.00

(including a 30 min **Afternoon Break**)

Session 2: Advanced Technologies

Chair: **David Dix**, Environmental Protection Agency, USA
Rapporteur: **James Bus**, Dow Chemical Company, USA
Recorder: **Rebecca Kauffman**, ICF International, Sweden

Description of parallel symposia and charge to participants (15 minutes)
- **David Dix**, Environmental Protection Agency, USA

Speakers: (30 minutes each with 15 minutes for discussion and Q&A)

Quantitative high-throughput screening of the Tox21 compound collection
- **Christopher Austin**, National Institutes of Health, USA

The EU-FP6 PredTox project: Using an integrated "omics" approach to mechanistic biomarker identification
- **Heidrun Ellinger-Ziegelbauer**, Bayer HealthCare AG, Germany

Toxicogenomics to improve prediction and risk assessment
- **George Daston**, Procter & Gamble, USA

The analysis of genomic dose-response data to define mode-of-action and low-dose behavior of chemical toxicants
- **Russell Thomas**, The Hamner Institutes for Health Sciences, USA

Parallel Symposium Sessions (continued)

14.00 – 17.00 (including a 30 min **Afternoon Break**)	Session 3: Risk Assessment *Chair:* **Richard Becker**, American Chemistry Council, USA *Rapporteur:* **Kathleen Plotzke**, Dow Corning Corporation, USA *Recorder*: **Kimberly Osborn**, ICF International, USA Description of parallel symposia and charge to participants (15 minutes) • **Richard Becker**, American Chemistry Council, USA *Speakers:* (30 minutes each with 45 minutes for discussion and Q&A) Computational systems biology and strategies for toxicity testing in the 21st century • **Melvin Andersen**, The Hamner Institutes for Health Sciences, USA What about exposure? • **Linda Sheldon**, Environmental Protection Agency, USA How may toxicogenomics improve risk assessment? • **Ursula Gundert-Remy**, Federal Institute for Risk Assessment, Germany
17.00 – 18.00	**Break and Aperitif**
18.00 – 19.00	**Reception and Poster Viewing**
19.00 – 21.00	**Group Dinner**

Tuesday, June 17, 2008

07.00 – 08.00	**Continental Breakfast**

Parallel Symposium Sessions / Panel Discussions

08.00 – 10.00

Session 1: Human Biomonitoring

Chair: **Ulrike Zimmer**, VCI, Germany
Rapporteur: **Herman Autrup**, University of Aarhus, Denmark
Recorder: **Ami Parekh**, ICF International, USA

Speakers: (30 minutes each, including Q&A)

Working backwards: Estimating exposure and risk from human biomonitoring data

- **Harvey Clewell**, The Hamner Institutes for Health Sciences, USA

Biomonitoring equivalents: Lessons learned and current status

- **Sean Hays**, Summit Toxicology, USA

Panel discussion (5-10 minute set-up by discussion leader listed below and then 10 minute group discussion for each question)

Discussion Leaders:

- **Ovnair Sepai**, Health Protection Agency, UK
- **Greet Schoeters**, Flemish Institute for Technological Research, Belgium
- **Peter Boogaard**, Shell International, The Netherlands

08.00 – 10.00

Session 2: Advanced Technologies

Chair: **David Dix**, Environmental Protection Agency, USA
Rapporteur: **James Bus**, Dow Chemical Company, USA
Recorder: **Rebecca Kauffman**, ICF International, Sweden

Panel discussion (5-10 minute set-up by discussion leader listed below and then 15-20 minute group discussion for each question)

Discussion Leaders:

- **Remi Bars**, Bayer CropScience, France
- **Timothy Gant**, University of Leicester, UK
- **Sandra Coecke**, European Commission Joint Research Center, Italy
- **James Bus**, Dow Chemical Company, USA
- **Melvin Andersen**, The Hamner Institutes for Health Sciences, USA

Parallel Symposium Sessions / Panel Discussions (continued)

08.00 – 10.00

Session 3: Risk Assessment

Chair: **Richard Becker**, American Chemistry Council, USA
Rapporteur: **Kathleen Plotzke**, Dow Corning Corporation, USA
Recorder: **Kimberly Osborn**, ICF International, USA

Speaker: (30 minutes including Q&A)

The path to integration of advanced technologies in risk assessment: Developments, opportunities and challenges

- **Bette Meek**, University of Ottawa, Canada

Panel discussion (5-10 minute set-up by discussion leader listed below and then 15-20 minute group discussion for each question)

Discussion Leaders:

- **Gerard Swaen**, The Dow Chemical Company, The Netherlands
- **Bette Meek**, University of Ottawa, Canada
- **Richard Becker**, American Chemistry Council, U.S
- **Elaine Cohen-Hubal**, Environmental Protection Agency, USA

10.00 – 10.30 **Morning Break**

Parallel Symposia Report Back

10.30 – 12.30

Chair: **Janet Mostowy**, Bayer MaterialScience, USA

Speakers: (30 minutes each, followed by discussion of interdisciplinary issues and Q&A)

- **Herman Autrup**, University of Aarhus, Denmark
- **James Bus**, Dow Chemical Company, USA
- **Kathleen Plotzke**, Dow Corning Corporation, USA

12.30 – 14.00 **Lunch**

Plenary Session III: Looking Ahead

14.00 – 15.20

Chair: **Timothy Gant**, University of Leicester, UK

Workshop outcomes and path ahead

- **Timothy Gant**, University of Leicester, UK

Speakers: (30 minutes each, including Q&A)

Risk assessment: A practical perspective

- **Lewis Smith**, Syngenta, UK

From data to policymaking

- **Peter Pärt**, European Commission Joint Research Centre, Italy

15.20 – 15.30

Workshop conclusions

- **Richard Phillips**, ExxonMobil, Belgium

15.30 – 16.00 **Afternoon Break**

ICCA-LRI Workshop
Twenty-First Century Approaches to Toxicity Testing, Biomonitoring, and Risk Assessment
June 16 and 17, 2008 at the Renaissance Amsterdam Hotel, The Netherlands
DRAFT Breakout Session Guide 04-03-08

Session 1: Biomonitoring

This session will explore the link from biomarkers of exposures to environmental exposures and how advancements in technologies (such as biological or environmental monitoring and modeling) can help make this connection and help interpret biomonitoring data. The aim is to showcase new developments or advancements in quantitative and qualitative interpretation and application of biomonitoring data.

Discussion Questions:

1. How do different organizations or groups that are responsible for public health decisions use biomonitoring data? How is information about the data being communicated?

2. How can biomonitoring data be used in the reconstruction of exposure (internal and external)?

3. How do epidemiological studies need to be re-thought/designed to facilitate collection of data that can support the use and interpretation of biomonitoring data?

4. How can biomonitoring data be made more useful for risk management?

ICCA-LRI Workshop
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Session 2: Advanced Technologies

This session will present new advances in hazard identification and dose-response assessment using genomics and high throughput testing/screening. We will discuss what information the various approaches will produce related to risk assessment and how this fits into the systems biology approach. The session goals are to understand the commonality and differences in the various programs, to identify areas for cooperation, to maximize value from the programs, and to identify a role for ICCA-LRI in addressing potential underemphasized areas.

Discussion Questions:

Current government funded programs are focused on either **priority setting** for further testing (EPA ToxCast) or **replacement/new definitive testing approaches** (intelligent testing strategies) without animals.

1. What are the areas of opportunity or concern regarding how the new technologies will facilitate either objective (i.e. prioritizing or replacement)? What is the role of reference standards and validation for these two approaches? What is value of dose/exposure information as foundational reference standards for application of technologies to hazard and risk characterization? What differences might be expected in the use of new technologies for informing the strategies of the two approaches?

2. When is more data too much data? What are our current limitations on data understanding and how does this impact on the application of new technologies within chemicals testing programs?

3. Where will the new technologies fit within the testing process in the future? Will there be applicability at several levels, e.g., stratification, genetic, mechanistic, target-organ identification, dose-response assessment, estimation of long-term adverse outcomes?

4. Can new technologies inform existing operation assumptions of toxicity testing and risk assessment, e.g., linear no-threshold evaluations for genotoxic substances, evaluation of hazards/risks of complex mixtures, use of traditional Maximum Tolerated Dose approaches to both *in vitro* and *in vivo* testing?

5. What is required to assure a sound scientific process in applying the data appropriately for these two approaches? What are the differences? What areas may need greater attention where ICCA LRI could contribute?

Other questions to consider:

6. What does chemical testing have to learn from application within the context of application to drug testing?

7. How can dose/exposure information available from biomonitoring activities impact development and application of new technologies for evaluation of environmental chemical hazard and risk? What types of exposure data from either human biomonitoring or animal toxicity tests will best inform interpretation of findings from the new technology models. How would such information refine the development and application strategies for these technologies?

8. Will the new technologies identify strategic directions beyond the two directions currently under evaluation, e.g., systems biology?

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DRAFT Breakout Session Guide 04-03-08

LRI

Session 3: Risk Assessment

During this session, we will discuss how applications of new technologies in biomonitoring and toxicity testing can assist in public health decision making and in communicating results to the medical community, the public, and the media.

This session aims to:

- Motivate a commitment to understanding and articulate the obligation to invest in the science necessary to take advantage of the potential opportunities that these advanced technologies and methods can offer.
- Address the seductive power of easily-generated voluminous-quantity data; reflecting on how much more powerful the data can be if its contextual relevance can be established.
- Invigorate the risk assessment community to modernize their framework and develop innovative tools to take advantage of these data and to provide their insights and input into other data/information that needs to be collected to render more value and meaning to the high-throughput data.

Discussion Questions:

1. Can the existing risk assessment framework take advantage of the data offered by new technologies?

2. How can we invigorate the risk assessment community to modernize their framework and develop innovative tools to take advantage of these data?

    a) Are there elements of the existing risk assessment framework that can inform or be used to develop a new framework?

    b) What are first steps in creating a new framework (i.e., where would we begin if we could start fresh)?

3. How do we ensure that a holistic systems approach is considered so that the data are not judged out of context?

4. From a regulatory perspective, how do these data enable us to protect individuals, especially those who are susceptible? As the technology advances, what are the considerations when developing individual risk profiles becomes possible?

国際的整合性を目指す有効性及び安全性に於ける遺伝子発現情報の標準化に関する研究

（H19-医薬-一般-001）

分担研究

- 菅野 純 （国立医薬品食品衛生研究所・安全性生物試験研究センター・毒性部）
  - mRNA測定標準化手法に関する調査研究総括・トキシコゲノミクスの標準化に関する調査研究
- 油谷 浩幸 （東京大学先端科学技術研究センターゲノムサイエンス部門 ゲノム科学）
  - 臨床におけるmRNA測定の標準化に関する調査研究
- 山口 照英 （国立医薬品食品衛生研究所・生物薬品部）
  - RNA等、基準物質の精度管理に関する調査研究
- 矢本 敬 （第一三共株式会社・安全性研究所）
  - 創薬過程でのmRNA測定の標準化に関する調査研究
- 住田 佳代 （住友化学株式会社・生物環境科学研究所・応用生物グループ）
  - 化学工業製品の安全性確保におけるmRNA測定の標準化に関する調査研究
- 山田 弘 （（独）医薬基盤研究所・ﾄｷｼｺｹﾞﾉﾐｸｽ・ｲﾝﾌｫﾏﾃｨｸｽﾌﾟﾛｼﾞｪｸﾄ）
  - トキシコゲノミクスの標準化に関する調査研究
- 宇山 佳明 （（独）医薬品医療機器総合機構 新薬審査第三部）
  - 医薬品審査過程におけるmRNA情報の標準化に関する調査研究

遺伝子発現(mRNA)測定技術(1)

- マイクロアレイ
  - 遺伝子発現解析ツールとしての市場シェアはAffymetrix > Agilentで変わらず
  - Exonアレイの性能向上については、現在、NIHSにおいてAffymetrixと協議中
  - DNAマイクロアレイ市場では住み分けが進んでいる？
    SNP～Affymetrix
    aCGH～Agilent

遺伝子発現(mRNA)測定技術(2)

- 次世代超高速シークエンサ
  並列に解読できるリード数を飛躍的に増大させることにより、トータルの塩基解読量を増やす方法
  - Illumina社　Solexa
  - ABI社　SOLiD
  - 454 LifeScience社　GS FLX

  市場シェア：Solexa > SOLiD >> GS FLX

  リード長：　GS FLX (250) > SOLiD (25～50) ≥ Solexa (25～36)

  塩基数/日：いずれも3億～5億　（cf. ABI社 3730xl　0.02億）

  - いずれの製品も前処理におけるバイアス発生や微量発現遺伝子への対応、スプライシングバリアントへの対応において技術的問題が残っている。
  - 導入時およびランニングにおける高コストも問題。

国際動向(1)

- MAQC II
  - face-to-face meetingを2回開催
  - MAQC-II Objective: Reaching consensus on the "best practices" (Data Analysis Protocol, DAP) in developing and validating microarray-based predictive models (classifiers) for clinical and preclinical applications.
  - 8th meeting (2008/3/24-26)
    (1) Present Data Analysis Protocols (DAPs) and analysis results
    (2)Discuss criteria for selecting MAQC's "candidate" model for each of the 13 endpoints from the six data sets
    (3) Discuss a plan for generating additional gene expression and genotyping data
    (4) Discuss manuscript topics, team leaders, and timeline.
  - 9th meeting (2008/9/18-19)
    (1) Report on the selection of MAQC-II "candidate" models
    (2) Analysis of prediction results on the validation sets
    (3) Progress report on the preparation of manuscripts
    (4) Timeline for the project and manuscript preparation >>> Apr~Jun, 2009

国際動向(2)

- ERCC
  - Telecon 8回開催 (1/15, 4/8, 6/17, 7/15, 8/19, 10/8, 10/30. 12/19)
  - Phase IV実施中
  - control配列の検証中(q-PCR, microarray)
  - control配列の評価のために生成したマイクロアレイデータ解析のために、2009/1末頃にface-to-face meetingを企画(延期の模様)
  - Phase V計画中
- Others
  - OECD

国内動向

- Percellome Project (NIHS)
  研究代表者より報告
- Toxicogenomics Project II (NIBIO)
  山田研究分担者より報告
- JMAC(バイオチップコンソーシアム)
  - 国内メーカーによるバイオチップビジネスのための標準化を企図
  - 経済産業省,NEDO海外調査事業
  - 2007/7活動開始
  - 2008年にはワーキンググループ会議を7回開催(内容不詳)

Percellome Project

- 強制経口(単回投与・反復投与 and/or 多臓器サンプリング):
  約100化合物の暴露実験を終了
- 吸入暴露(単回暴露・反復暴露):10化合物終了
- 発生時暴露、暴露後の行動影響等についても推進中
- データの一部公開(6化合物、2006/6～、
  登録ユーザー数 延べ102名)
  - 現行システムは使用終了。in house開発に移行する計画
  - MAQC/ERCCコンソーシアムメンバーに用途制限付きでフルアクセス解放
    >>> 発言権の強化を図る
  - 標準スパイクRNA mixture(GSC)の供給体制の整備

Application of Toxicogenomics in Safety Evaluation and Risk Assessment

Publisher- John Wiley and Sons Inc.

Editors: Darrell R Boverhof and B. Bhaskar Gollapudi

- Standardization of gene expression information for the safety evaluation - Activities in Japan -
- Ken-ichi Aisaki, MD, PhD, and Jun Kanno, M.D., Ph.D.
- Division Head, Division of Cellular and Molecular Toxicology, Biological Safety Research Center, National Institute of Health Sciences.
- Correspondance:
- Jun Kanno: e-mail kanno@nihs.go.jp

OECD

SECOND SURVEY ON AVAILABLE OMICS TOOLS

(draft August 2008)

1. This paper is intended to provide information on the current approaches in toxicogenomics.
2. Omics study can provide genome-wide information and it is expected that, through systematic efforts to generate mechanistic information using omics technologies, diagnostic and predictive assessments of hazardous chemicals can be established for risk assessment.
3. In the preparation for the OECD/IPCS Workshop on Toxicogenomics in Kyoto on 13-15 November 2004, the OECD Secretariat conducted a survey of existing toxicogenomic tools in member countries (Kyoto Survey). This survey was mainly focused on ecotoxicogenomics and the result was circulated at the Workshop (see Annex 4).
4. In view of this situation, the OECD/IPCS Advisory Group on Toxicogenomics agreed to follow-up current approaches in toxicogenomics in OECD member countries.

ANNEX 2: SUMMARY OF THE 2006 SURVEY RESPONSES *

Common name of the species	Genome sequence been defined?	Number of expression sequence tags or genes sequenced	the method include a microarray? (If yes, platform of the microarray (Custom /Commercial))	proteomics? (If yes, information on the technology)	metabolomics? (If yes, information on the technology)	other technologies? (If yes, information on the technology)	Scale (Number of genes, proteins or chemicals that can be analyzed)	Chemicals studied	Publications	Organization and Country
Mouse (C57B L/6Cr ela)	Faciliat e		Yes (Affymetrix GeneChip Mouse Genome 430A, Mouse Genome 430-2)	No	No	Yes ("Percellome method" to normalize transcriptome data to cell number of the sample (mRNA copy number per cell))	Ca. 45,000 probe set data, finished up to 90 chemicals (See Annex 4 for more detail.)	1,2-dichloro-3-nitrobenzene, 1[6-1-2-3-nitrol, etc. (See Annex 4 for more detail.)	Yes	National Institute of Health Sciences, Japan
Medaka	No		Yes (Custom cDNAarry for brain of medaka, Medaka embryo array (Kragenomics Co, LTD)	No				tributyltin, PCBs, mixture of TBT and PCBs	in preparing	Faculty of Agriculture, Kyushu University, Japan
Rat (White Wistar)	in progress	More than 90% of the estimated 2.8 Gb genome is available (state August 2006)	Yes (GeneChip Rat Genome 230 2.0 Array, (Affymetrix))	Yes (2D-DiGE, Proteinlab (SELDI-MS))	No	No	genomics: 31,000 probe sets, 28,000 rat genes; proteomics: approx. 1000 annotated protein spots (work in progress)	N-nitrosodiethylamine (NDEA), Allitenin 31 etc. (See Annex 4 for more detail.)		BfR, Germany

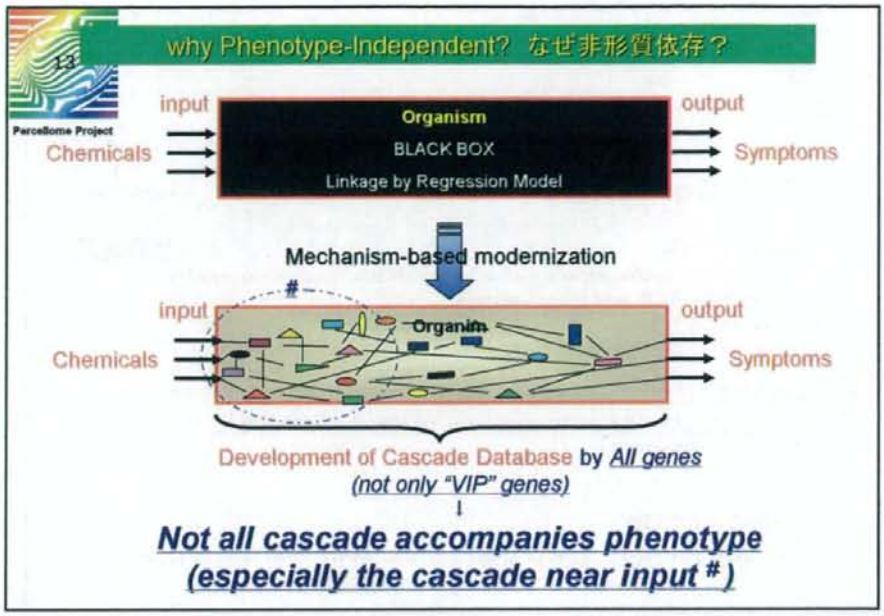
MHLW* Toxicogenomics Projects

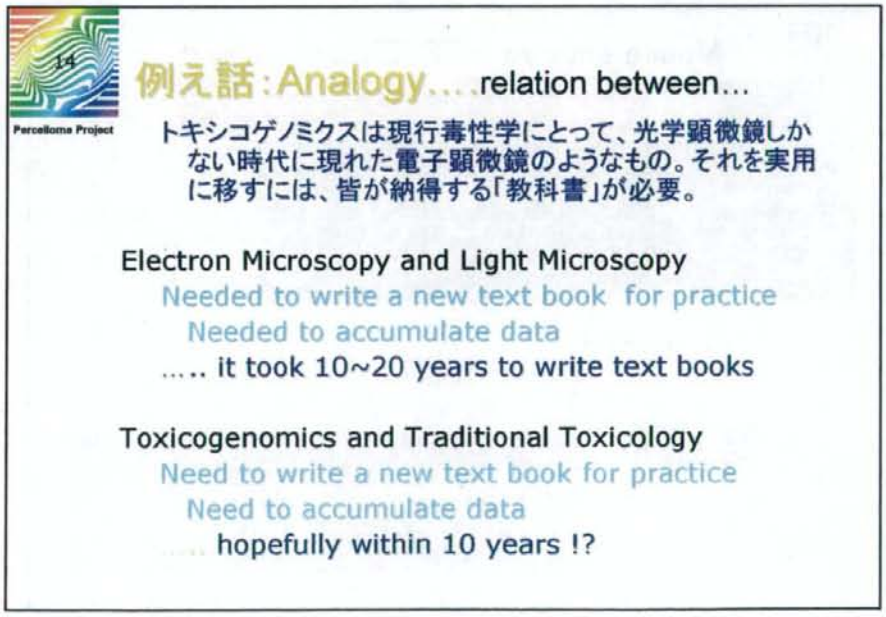
*Ministry of Health Labour and Welfare

Percellome Project

- Toxicogenomics Project (2002~2006, 5y)
  NIHS +17 Pharmaceuticals
  - rat (oral; liver, kidney) 150 chem, single/ repeat exposure
  - + In vitro (rat primary hepatocyte, human primary hepatocyte)
  - Now @ Nat'l Institute of Biomedial Innovation (Osaka) 2005~2006
  - 2nd round project at Osaka (2007~2011), mainly for further data analysis

- Percellome Project (Mouse)
  Chemical Safety Database
  - Div. Cellular and Molecular Toxicology/ BSRC/ NIHS
    - TTG1: 2003~2005 (single exposure), oral. liver 90 chem(肝＋α)
    - ITG: 2005~2007 Inhalation Toxicogenomics(吸入)
    - TTG2: 2006~2008 (repeated exposure, multi-organ etc.), oral (反復暴露・多臓器連関)
    - FTG: 2004~ Fetus (developmental)(胎児・発生)
    - NTG: 2006~ Behavior -> Brain TG (HC, BS, Cx, Cl) (行動神経・脳(大脳・脳幹部・海馬・小脳))
    - Food TG: 2007~ Functional Health Food (CoQ10, α-lipo), food ingredient(食品開連)
    - Nano・PM*TG:2007~ Asbestos, Multiwall Carbon Nanotube, Fullerene (腹膜中皮) *PM:粒子状物質 particulate matter


13
Percellome Project
why Phenotype-Independent? なぜ非形質依存？
input
Chemicals
Organism
BLACK BOX
Linkage by Regression Model
output
Symptoms
Mechanism-based modernization
#
input
Chemicals
Organism
output
Symptoms
Development of Cascade Database by All genes
(not only "VIP" genes)
Not all cascade accompanies phenotype
(especially the cascade near input #)


14
Percellome Project
例え話：Analogy…. relation between…
トキシコゲノミクスは現行毒性学にとって、光学顕微鏡しかない時代に現れた電子顕微鏡のようなもの。それを実用に移すには、皆が納得する「教科書」が必要。
Electron Microscopy and Light Microscopy
Needed to write a new text book for practice
Needed to accumulate data
….. it took 10~20 years to write text books
Toxicogenomics and Traditional Toxicology
Need to write a new text book for practice
Need to accumulate data
…. hopefully within 10 years !?

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Percellome Project

BMC Genomics

BioMed Central

Methodology article

Open Access

"Per cell" normalization method for mRNA measurement by quantitative PCR and microarrays

Jun Kanno*†1, Ken-ichi Aisaki†1, Katsuhide Igarashi1, Noriyuki Nakatsu1, Atsushi Ono1, Yukio Kodama1 and Taku Nagao2

Address: 1Division of Cellular and Molecular Toxicology, National Institute of Health Sciences, 1-18-1, Kamiyoga, Setagaya-ku, Tokyo 158-8501, Japan and 2President, National Institute of Health Sciences, 1-18-1, Kamiyoga, Setagaya-ku, Tokyo 158-8501, Japan

Email: Jun Kanno* - kanno@nihs.go.jp; Ken-ichi Aisaki - aisaki@nihs.go.jp; Katsuhide Igarashi - igarashi@nihs.go.jp; Noriyuki Nakatsu - n-nakatsu@nihs.go.jp; Atsushi Ono - Atsushi@nibio.go.jp; Yukio Kodama - kodama@nihs.go.jp; Taku Nagao - nagao@nihs.go.jp

* Corresponding author †Equal contributors

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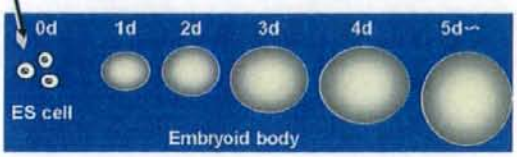
Percellome Project

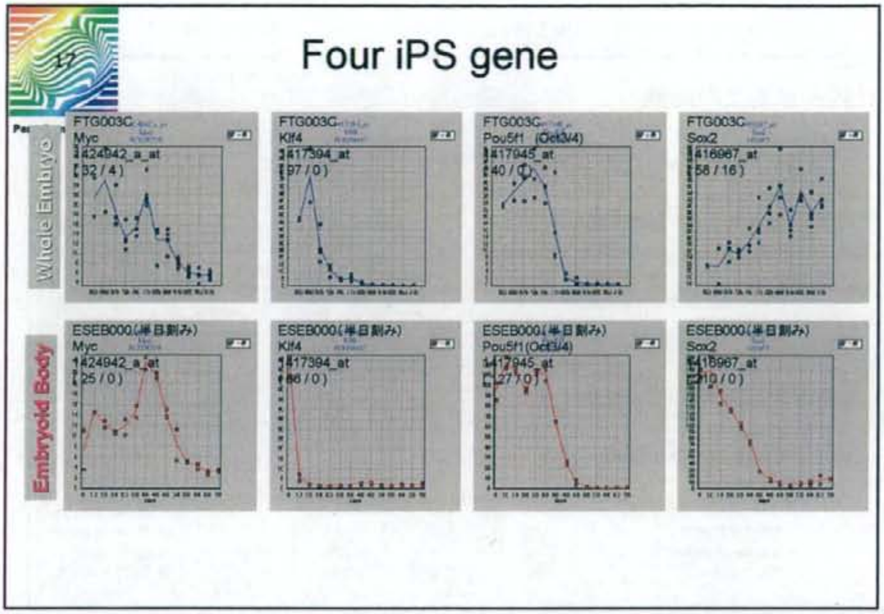
Mouse embryo – ES/EB comparison

In vivo

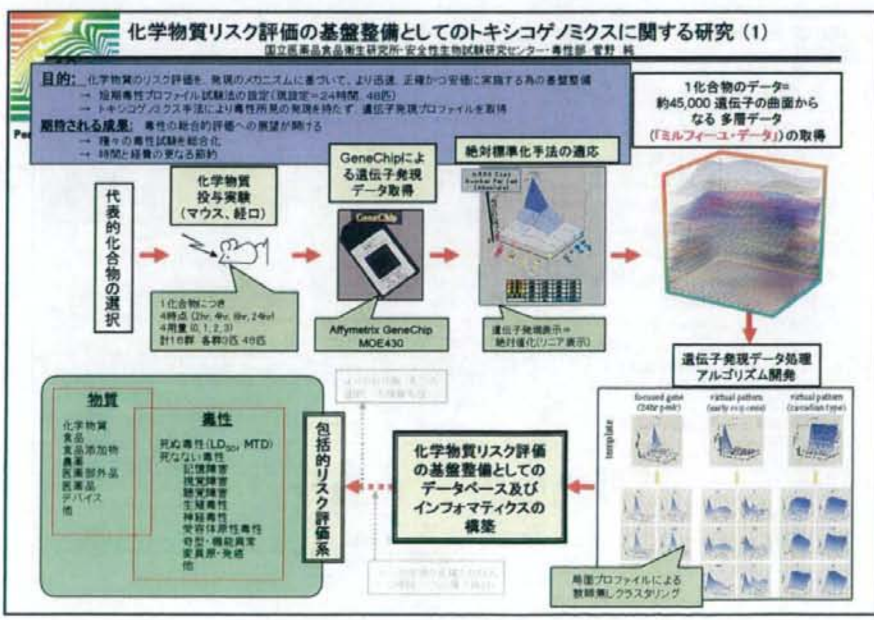
To cover implantation stage where direct analysis on embryo is difficult

In vitro





Four iPS gene
Whole Embryo
Embryoid Body
FTG003C
Myc
1424942_a_at
FTG003C
Klf4
1417394_at
FTG003C
Pou5f1 (Oct3/4)
1417945_at
FTG003C
Sox2
1416967_at
ESEB000(半日刻み)
Myc
1424942_a_at
ESEB000(半日刻み)
Klf4
1417394_at
ESEB000(半日刻み)
Pou5f1(Oct3/4)
1417945_at
ESEB000(半日刻み)
Sox2
1416967_at



化学物質リスク評価の基盤整備としてのトキシコゲノミクスに関する研究 (1)
国立医薬品食品衛生研究所･安全性生物試験研究センター･毒性部 菅野 純
目的: 化学物質のリスク評価を、発現のメカニズムに基づいて、より迅速、正確かつ安価に実施する為の基盤整備
→ 短期毒性プロファイル試験法の設定(現設定=24時間、48匹)
→ トキシコゲノミクス手法により毒性所見の発現を待たず、遺伝子発現プロファイルを取得
期待される成果: 毒性の総合的評価への展望が開ける
→ 種々の毒性試験を総合化
→ 時間と経費の更なる節約
1化合物のデータ=
約45,000 遺伝子の曲面から
なる 多層データ
(「ミルフィーユ・データ」)の取得
代表的化合物の選択
化学物質
投与実験
(マウス、経口)
1化合物につき
4時点 (2hr, 4hr, 8hr, 24hr)
4用量 (0, 1, 2, 3)
計16群 各群3匹 48匹
GeneChipによる遺伝子発現データ取得
Affymetrix GeneChip
MOE430
絶対標準化手法の適応
遺伝子発現表示=
絶対値化(リニア表示)
遺伝子発現データ処理
アルゴリズム開発
局面プロファイルによる
教師無しクラスタリング
化学物質リスク評価
の基盤整備としての
データベース及び
インフォマティクスの
構築
包括的リスク評価系
物質
化学物質
食品
食品添加物
農薬
医薬部外品
医薬品
デバイス
他
毒性
死ぬ毒性(LD50, MTD)
死なない毒性
記憶障害
視覚障害
聴覚障害
生殖毒性
神経毒性
受容体原性毒性
奇型・機能異常
変異原・発癌
他