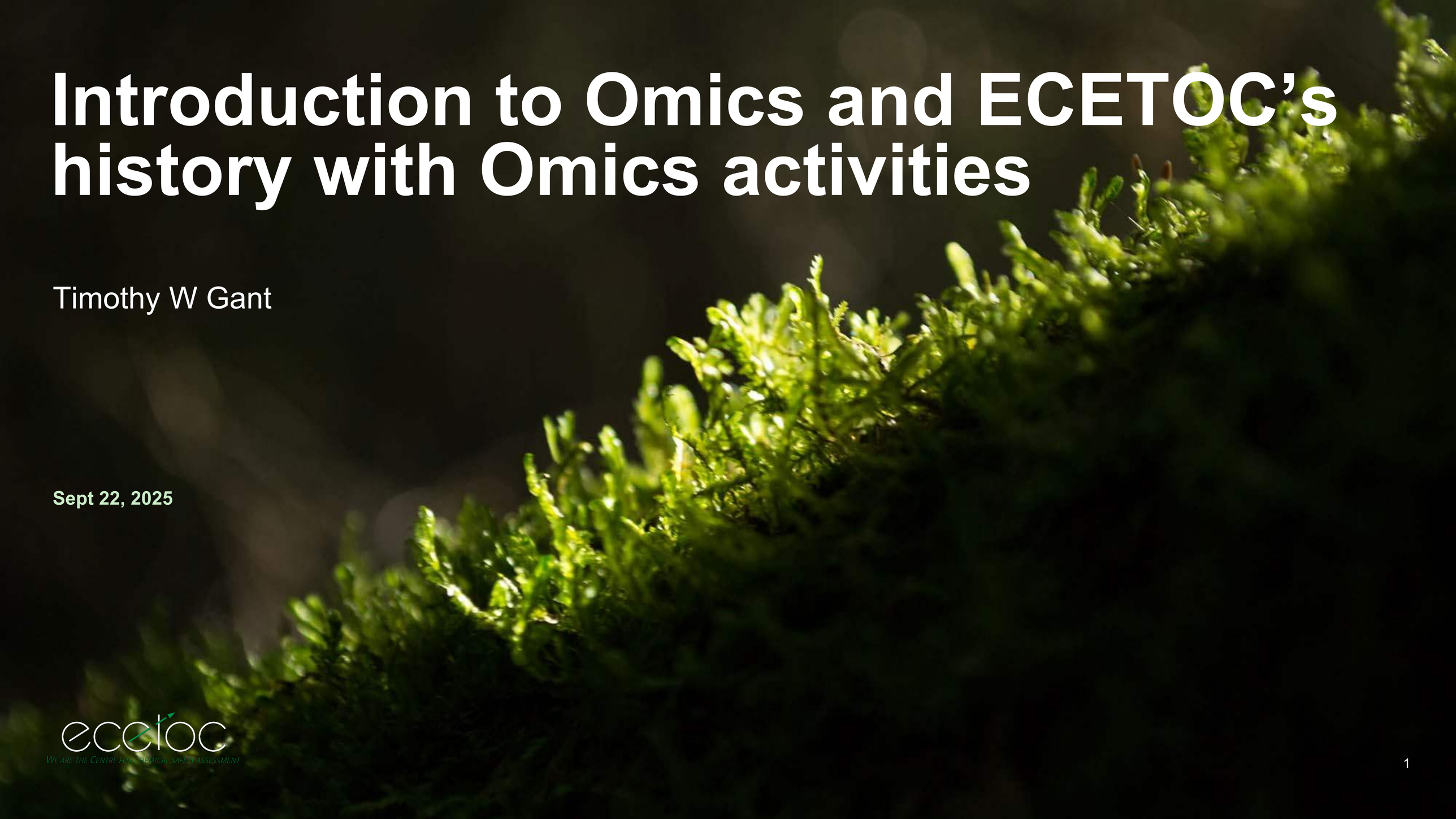
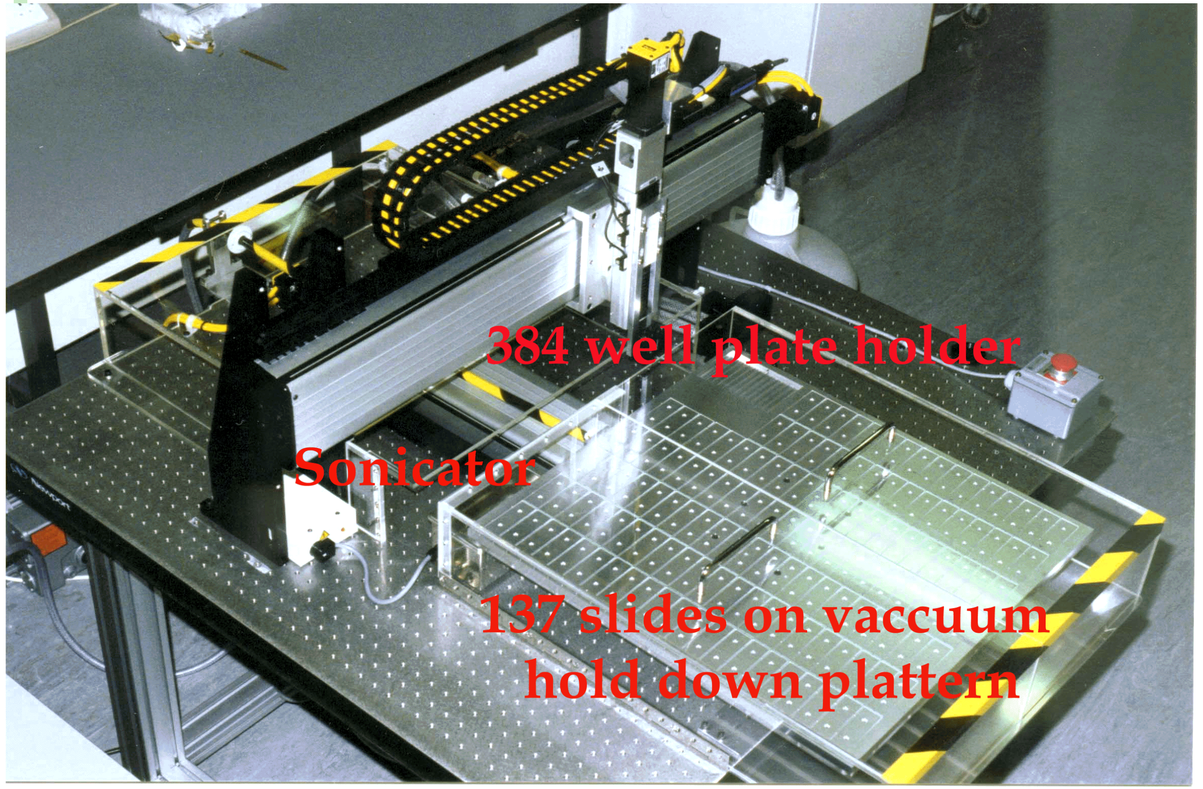
Introduction to Omics and ECETOC's history with Omics activities

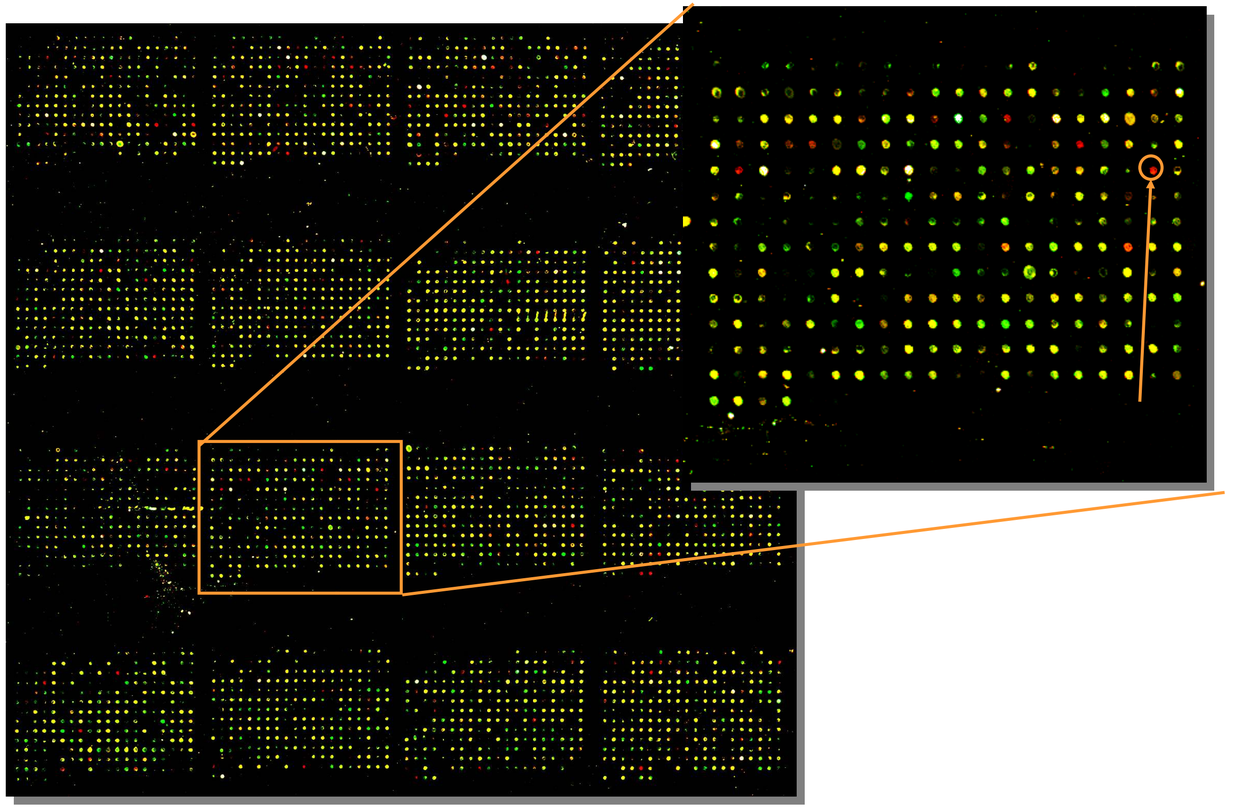
Timothy W Gant

Sept 22, 2025



1999 – 2000 Getting into Genomics : Leicester, NIEHS, UCSF





2007 – ECETOC technical meeting: Brussels

ecetoc

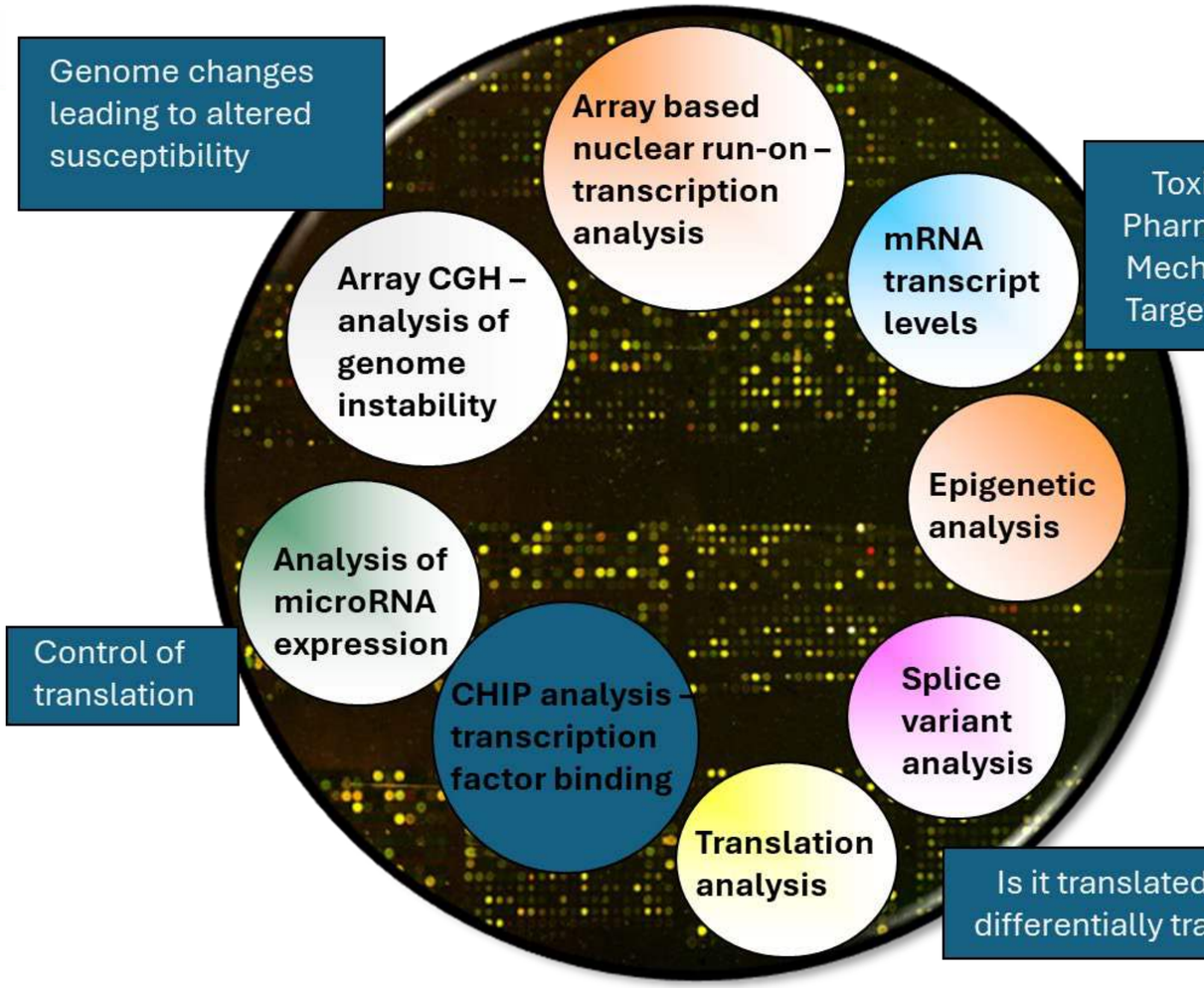
ANNUAL TECHNICAL MEETING

Programme

Part I: Genomics

Part II: Nanoparticles

10th May 2007
Crowne Plaza Hotel, Brussels Airport
09.00 – 16.00



2007 – ECETOC mutagenesis methods workshop: Malta

Workshop on the Refinement of Mutagenicity / Genotoxicity Testing
23-24 April 2007, Malta

Workshop Report No. 9

Brussels, September 2007

Dr. Gant gave a presentation on the **potential application of toxicogenomics to mutagenicity / genotoxicity testing**. He explained that genomics has been part of the toxicologists toolbox for nearly a decade. During that time there has been much excitement and expectation of its potential to inform on molecular toxicity particularly using *in vitro* systems and over shorter time periods of exposure. To date, general expectation has been greater than delivery and this has led to some disillusionment and frustration with the technique[5]. To a very large extent this has been driven by: (i) exaggerated expectation, (ii) underestimation of the sheer complexity of the data and analysis required, (iii) difficulty in variable control and (iv) inappropriate experimental design. Recent data from the US FDA has indicated a large proportion of the technical variability has been controlled. Concurrent with technical improvement there has been a proliferation of bioinformatic tools. These have increased the ease of data analysis but also its complexity in terms of choice of analysis methods. We are now at a position, where as many of the technical barriers to effective implementation have been overcome, exploration of the true toxicological applicability of the technique can commence. Careful experimental design and considered bioinformatics will always be required.

2007 – ECETOC workshop on the application of Omic Technologies : Malaga (the first one)

Workshop on the
Application of 'Omic Technologies i
Toxicology and Ecotoxicology:
Case Studies and Risk Assessment
6-7 December 2007, Malaga

Workshop Report No. 11

Brussels, July 2008

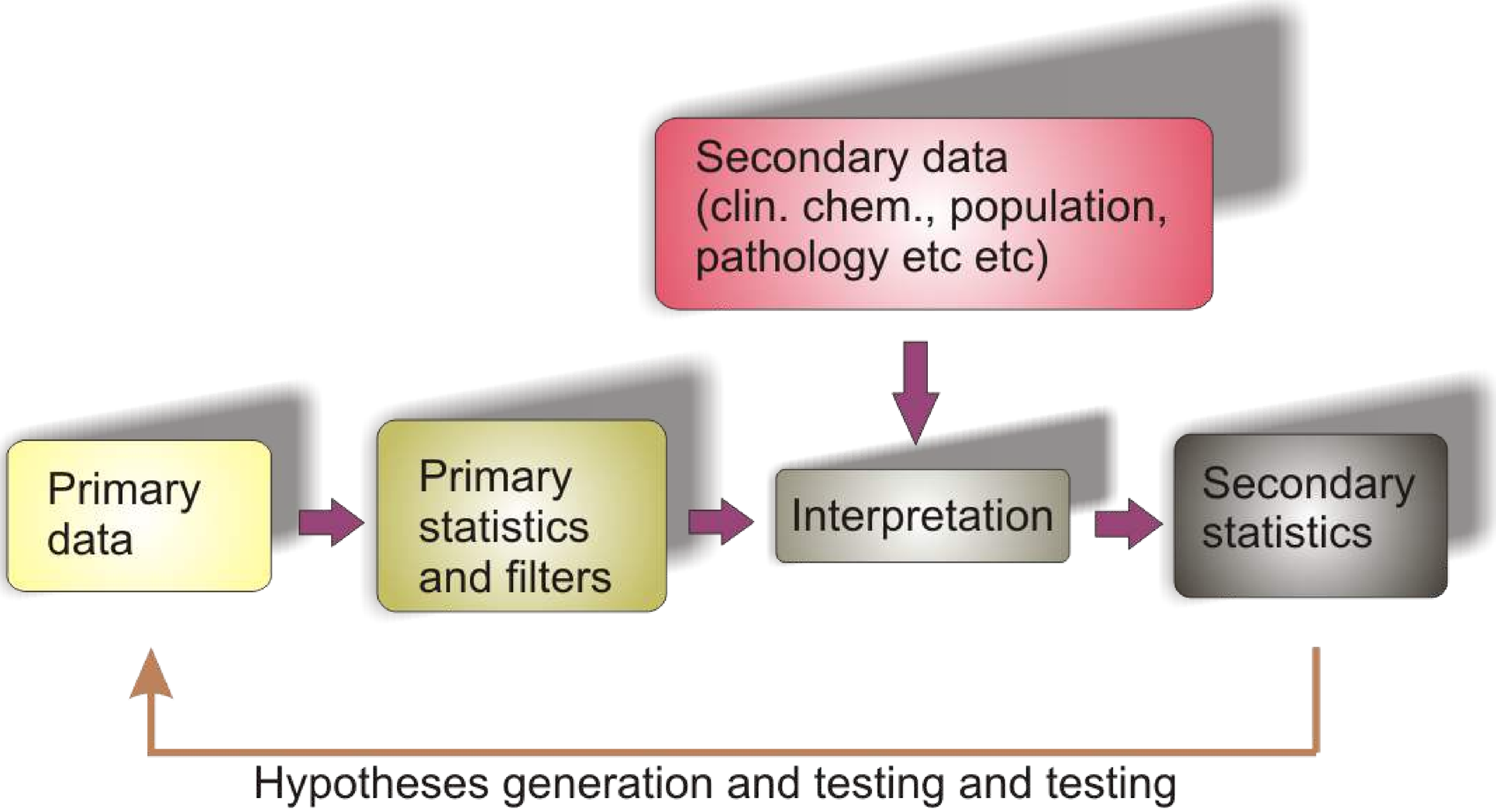
3.4 Genomic data interpretation

T. W. Gant
Medical Research Council, University of Leicester

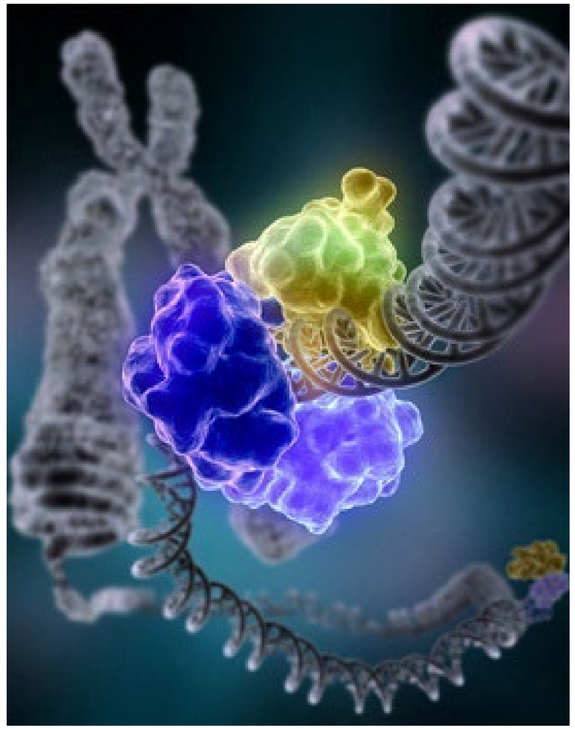
Introduction

Interpretation of genomics data is the key factor to its successful application in a translational context. Interpretation though often proves to be the most time consuming and challenging area of genomic science. The advent of many more reproducible platforms has made less complex the process of generating data, but has also increased the rate at which the data can be generated. This has had the effect of magnifying the problem of data interpretation by a factor roughly equivalent to the rate at which the data are generated. Further complexity is added by the explosion in online access to associated data as many new data streams have to be incorporated into a meaningful analysis. Genomics in particular but also other high throughput analysis have taken us from a point where the analysis of data, for example expression of gene x altered by exposure to chemical a in biological system b, could be achieved virtually at the point of data generation, to a new point where the data analysis may not be completed for many months or even years downstream.

2007-The analysis flow and bioinformatic methods



2008 – ECETOC workshop on Significance of DNA adducts : Cavtat



WORKSHOP PROGRAMME

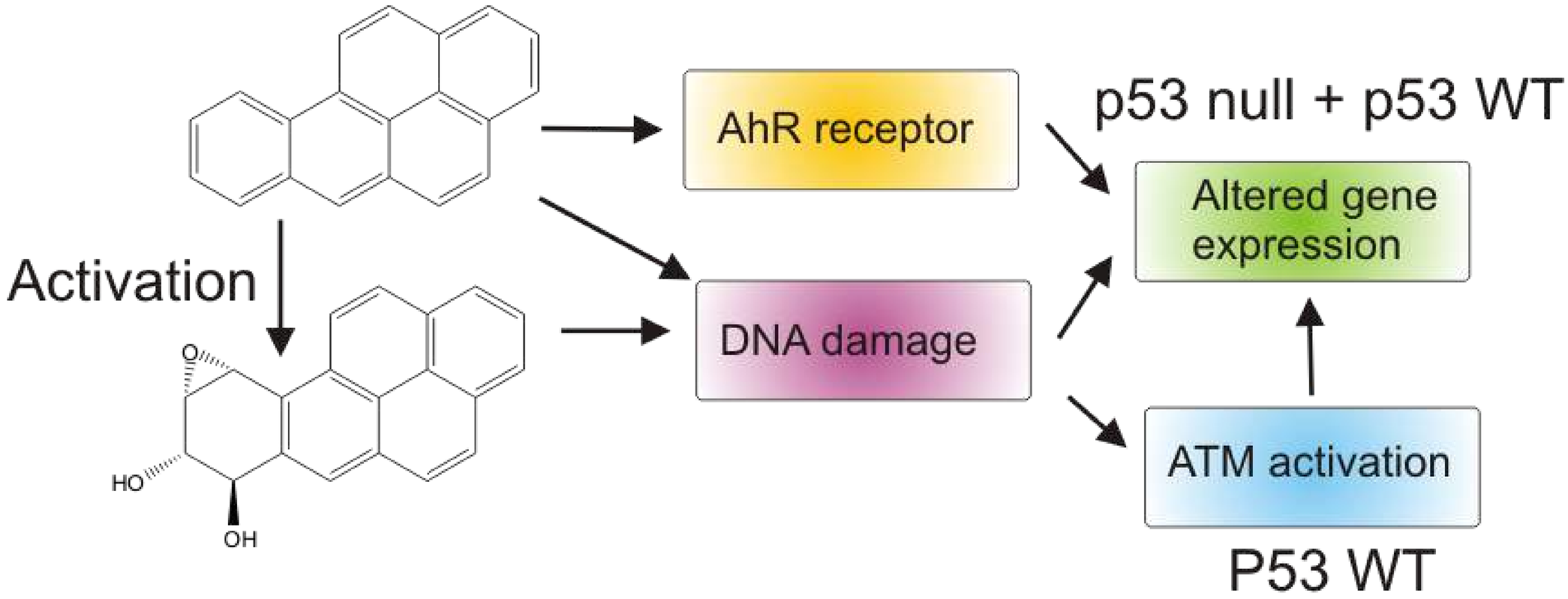
Workshop on the Biological Significance of DNA Adducts: Part II

25-26 September 2008
Cavtat, Croatia

In co-operation with ILSI/HESI DNA Adduct Project Committee
Sponsored by

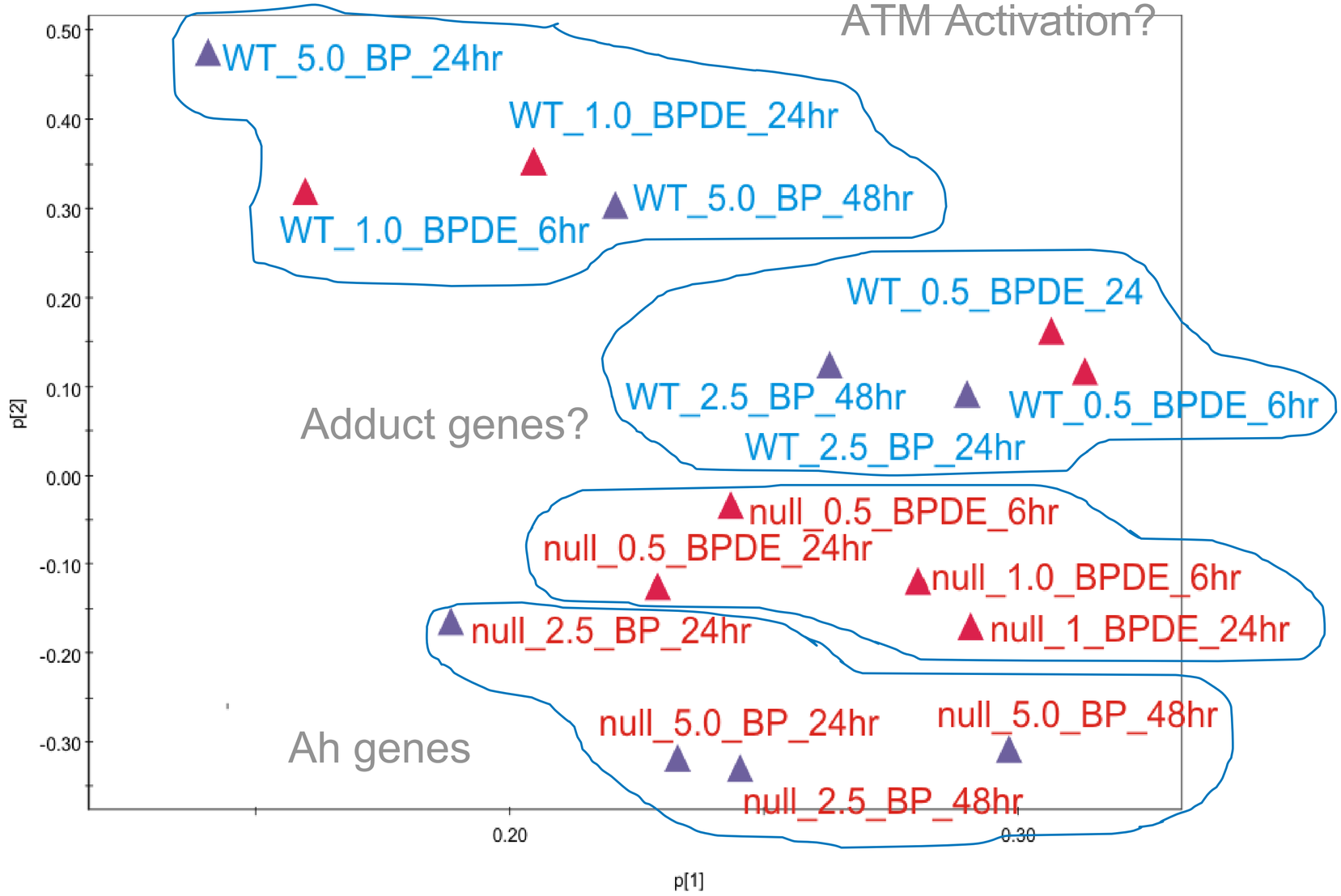
Joint Industry Group
(CEFIC LO, EO & Der., and PO & Glycols SGs and ACC Olefins E/PWG, and EO/EG Panels)

2008 - Cavtat



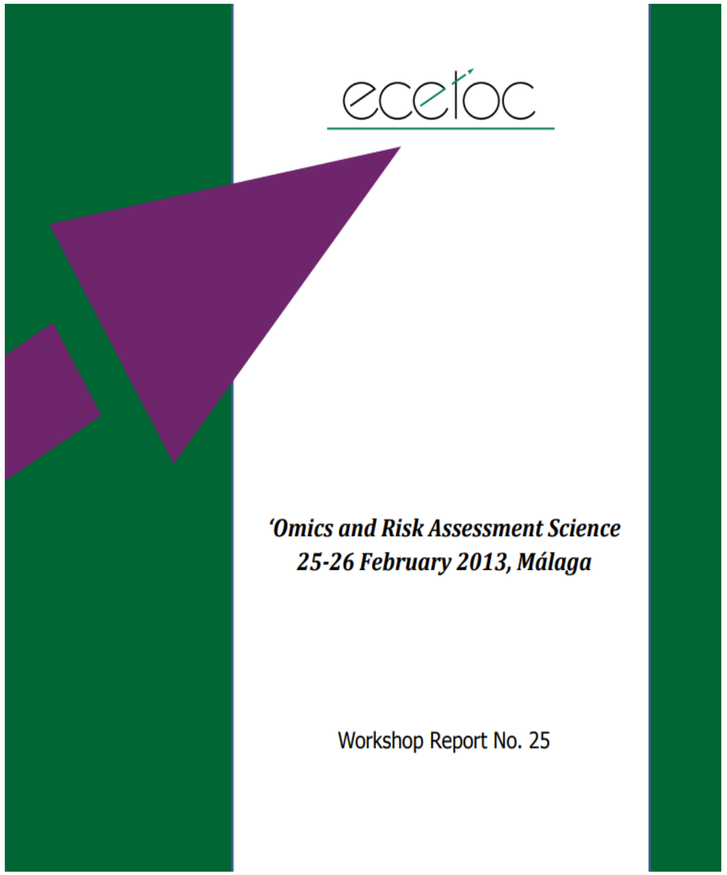
GEO Omnibus accession – GSE9547

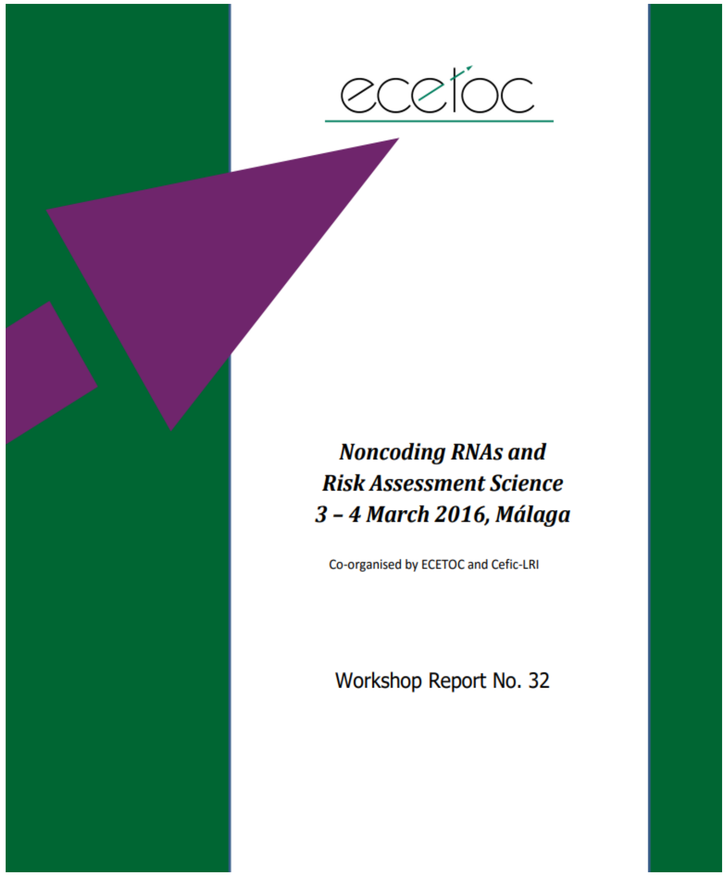
2008 - Cavtat



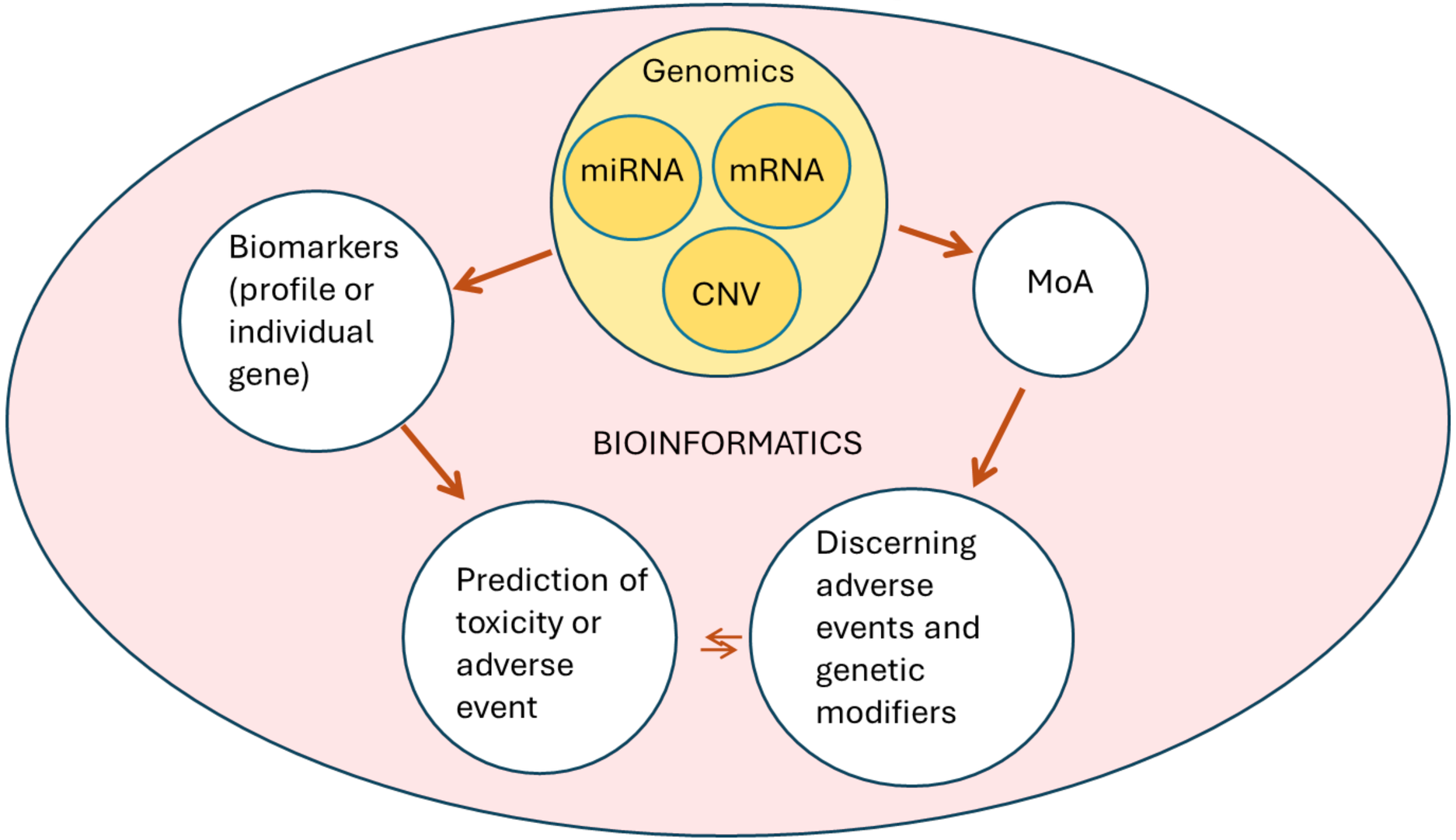
ecetoc
We are the Centre for chemical safety assessment

2010 & 2013 & 2016 : The Further Malaga meetings

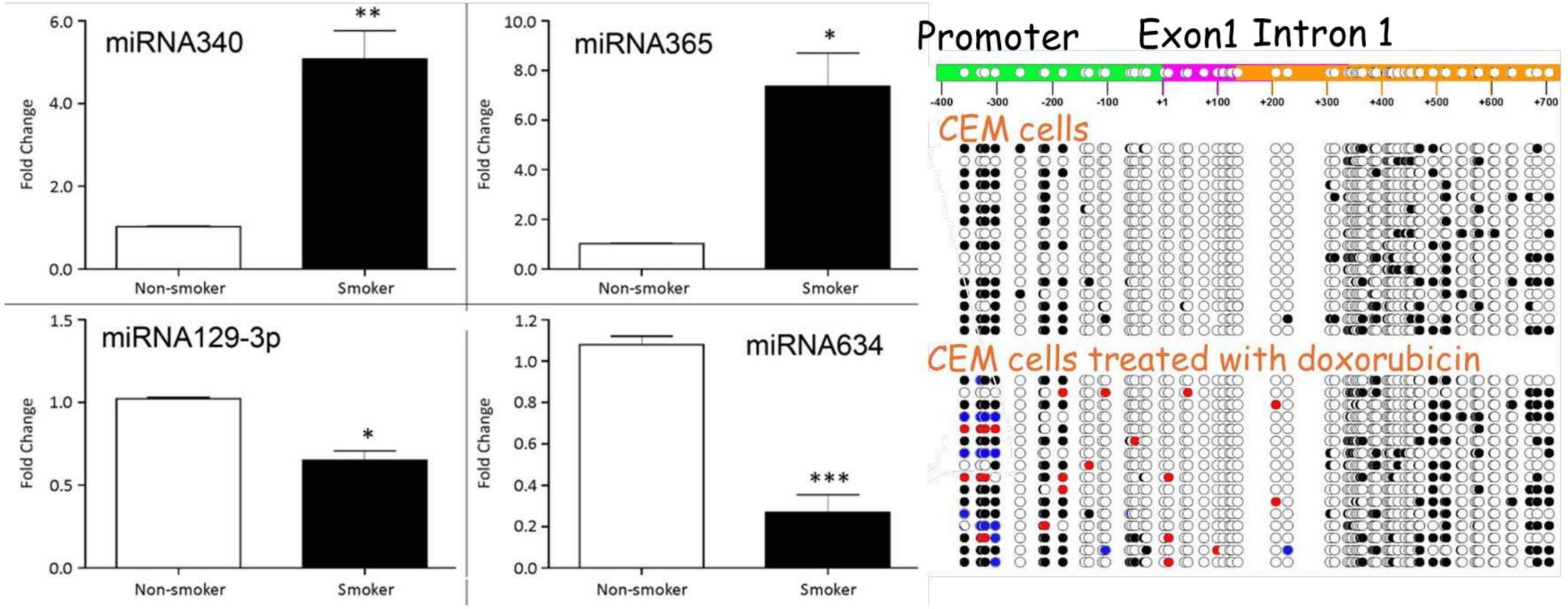




2010 - Key drivers for the application of genomics in chemical risk assessment : Malaga

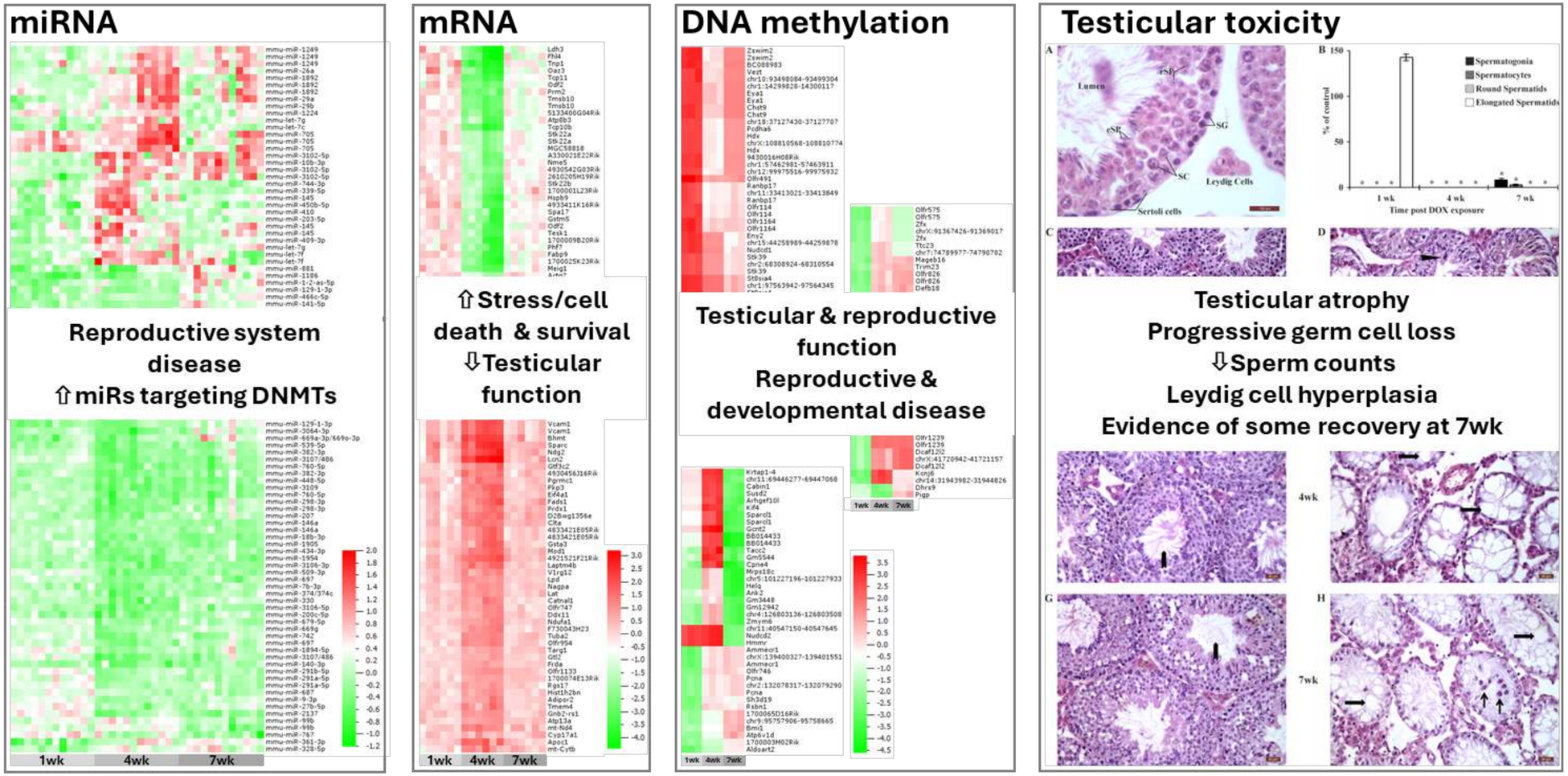


2013 - miRNAs and methylation as markers of exposure : Malaga



Marczylo *et al* Epigenetics 7, 1 (2012)

2016 – Hazard – Phenotypic anchoring : Malaga

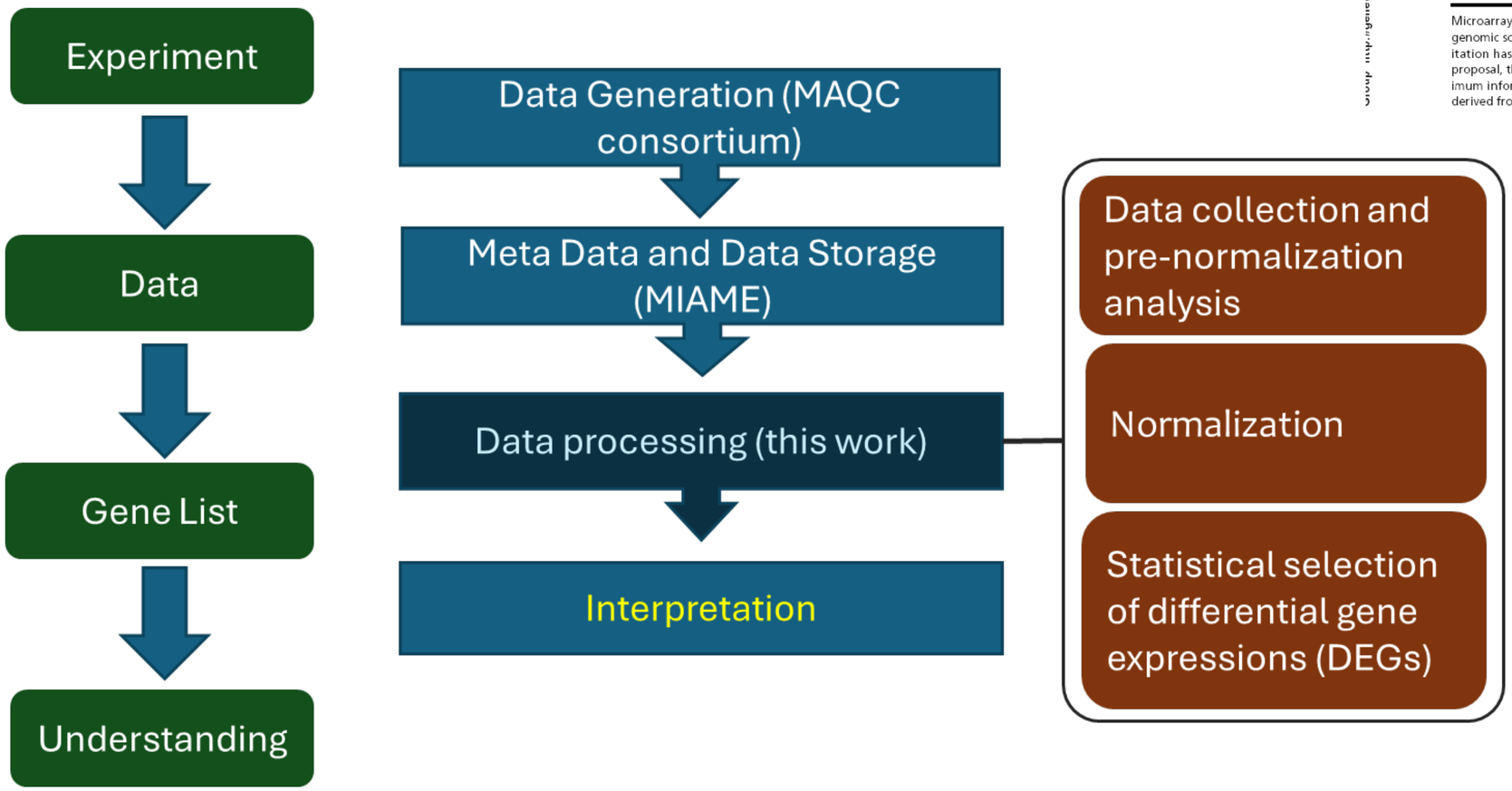


Correlation of ncRNA (miRNA) expression profiles with other profiles (mRNA/DNA methylation) and phenotypic endpoints (testicular toxicity) following chronic DOX.

2015 & 2016 - meetings to consider standard methods for data analysis : Brussels

- David Rouquié, France
- Mohamed Benahmed, UNICE, France
- Timothy Ebbels, Imperial College London, UK
- Karma Fussell, Nestlé, Switzerland
- Tim Gant, CRCE, UK
- Madeleine Laffont, ECETOC, Belgium
- Alan Poole, ECETOC, Belgium
- Steffen Schneider, BASF, Germany
- Leming Shi, NCTR/FDA, USA
- Weida Tong, NCTR/FDA, USA
- Shu-Dong Zhang, Queen's Univ. Belfast, N. Ireland

2015 & 2016 : Brussels - Work Area



Minimum information about a microarray experiment (MIAME)—toward standards for microarray data

Alvis Brazma[1], Pascal Hingamp[2], John Quackenbush[3], Gavin Sherlock[4], Paul Spellman[5], Chris Stoeckert[6], John Aach[7], Wilhelm Ansorge[8], Catherine A. Ball[4], Helen C. Causton[9], Terry Gaasterland[10], Patrick Glenisson[11], Frank C.P. Holstege[12], Irene F. Kim[4], Victor Markowitz[13], John C. Matese[4], Helen Parkinson[1], Alan Robinson[1], Ugis Sarkans[1], Steffen Schulze-Kremer[14], Jason Stewart[15], Ronald Taylor[16], Jaak Vilo[1] & Martin Vingron[17]

Microarray analysis has become a widely used tool for the generation of gene expression data on a genomic scale. Although many significant results have been derived from microarray studies, one limitation has been the lack of standards for presenting and exchanging such data. Here we present a proposal, the Minimum Information About a Microarray Experiment (MIAME), that describes the minimum information required to ensure that microarray data can be easily interpreted and that results derived from its analysis can be independently verified. The ultimate goal of this work is to establish a

CEFIC/LRI C4 project

2016 – Key meeting; Omics in Risk Assessment : Madrid

ecetoc

ECETOC WORKSHOP

Applying 'Omics Technologies in Chemicals Risk Assessment

10-12 October, 2016
NH Nacional Hotel, Madrid, Spain

Objectives:

1. With representatives from European Commission; the OECD; US-EPA; US-FDA - share and update frameworks developed by ECETOC multi-expert teams on how to aquire, analyse and apply 'omics data. Ensue fitness for purpose.
2. Generate consensus of opinion on the steps needed to achieve best practices for applying 'omics technologies in chemicals risk assessment.

***Toics covered** (Room Documents distributed prior to the workshop):*

- ✓ Establishing GLP-like Context for Collecting, Storing and Curating 'Omics Data
- ✓ Best Practices for Analysisng 'Omics Data
- ✓ Best Practices for WoE Approaches for Integrating 'Omics Data
- ✓ Best Practices for Establishing Pathways to Connect Results of 'Omic Data to Phenotype

Outcomes – Reporting and Weight of Evidence Frameworks

Regulatory Toxicology and Pharmacology xxx (2017) 1–13

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

The challenge of the application of 'omics technologies in chemicals risk assessment: Background and outlook

Ursula G. Sauer [a], Lize Deferme [b], Laura Gribaldo [c], Jörg Hackermüller [d], Tewes Tralau [e], Ben van Ravenzwaay [f], Carole Yauk [g], Alan Poole [h], Weida Tong [i], Timothy W. Gant [j, *]

[a] Scientific Consultancy – Animal Welfare, Germany
[b] ExxonMobil Petroleum and Chemical, Belgium
[c] European Commission, Joint Research Centre, European Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM), Italy
[d] Department of Molecular Systems Biology, Helmholtz Centre for Environmental Research - UFZ, Germany
[e] Department of Chemical and Product Safety, German Federal Institute of Risk Assessment (BfR), Germany
[f] BASF SE, Germany
[g] Environmental Health Science and Research Bureau, Health Canada, Canada
[h] European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC), Belgium
[i] National Center for Toxicological Research (NCTR), U.S. Food and Drug Administration (FDA), USA
[j] Centre for Radiation, Chemical and Environmental Effects (CRCE), Harwell Science and Innovation Campus, Public Health England (PHE), UK

Regulatory Toxicology and Pharmacology 91 (2017) S46–S60

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

Framework for the quantitative weight-of-evidence analysis of 'omics data for regulatory purposes

Jim Bridges [a, *], Ursula G. Sauer [b], Roland Buesen [c], Lize Deferme [d], Knut E. Tollefsen [e], Tewes Tralau [f], Ben van Ravenzwaay [c], Alan Poole [g], Mark Pemberton [h]

[a] Surrey University, UK
[b] Scientific Consultancy – Animal Welfare, Germany
[c] BASF SE, Germany
[d] ExxonMobil Petroleum and Chemical, Belgium
[e] Norwegian Institute for Water Research (NIVA), Norway
[f] Department of Chemical and Product Safety, German Federal Institute of Risk Assessment (BfR), Germany
[g] European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC), Belgium
[h] Systox Ltd., UK

ARTICLE INFO

Article history:
Received 7 July 2017
Received in revised form
11 October 2017
Accepted 12 October 2017
Available online 14 October 2017

Keywords:

ABSTRACT

A framework for the quantitative weight-of-evidence (QWoE) analysis of 'omics data for regulatory purposes is presented. The QWoE framework encompasses seven steps to evaluate 'omics data (also together with non-'omics data): (1) Hypothesis formulation, identification and weighting of lines of evidence (LoEs). LoEs conjoin different (types of) studies that are used to critically test the hypothesis. As an essential component of the QWoE framework, step 1 includes the development of templates for scoring sheets that predefine scoring criteria with scores of 0–4 to enable a quantitative determination of study quality and data relevance; (2) literature searches and categorisation of studies into the pre-

Regulatory Toxicology and Pharmacology 91 (2017) S36–S45

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

A generic Transcriptomics Reporting Framework (TRF) for 'omics data processing and analysis

Timothy W. Gant[a,*], Ursula G. Sauer[b], Shu-Dong Zhang[c], Brian N. Chorley[d], Jörg Hackermüller[e], Stefania Perdichizzi[f], Knut E. Tollefsen[g], Ben van Ravenzwaay[h], Carole Yauk[i], Weida Tong[j], Alan Poole[k]

[a] Centre for Radiation, Chemical and Environmental Hazards (CRCE), Public Health England (PHE), Harwell Campus, Oxfordshire, UK
[b] Scientific Consultancy – Animal Welfare, Germany
[c] Northern Ireland Centre for Stratified Medicine, Biomedical Sciences Research Institute, University of Ulster, UK
[d] U.S. Environmental Protection Agency, USA
[e] Department of Molecular Systems Biology, Helmholtz Centre for Environmental Research - UFZ, Germany
[f] Center for Environmental Toxicology, Agency for Prevention, Environment and Energy (Arpae), Emilia-Romagna, Italy
[g] Norwegian Institute for Water Research (NIVA), Norway
[h] BASF SE, Germany
[i] Environmental Health Science and Research Bureau, Health Canada, Canada
[j] National Center for Toxicological Research (NCTR), U.S. Food and Drug Administration (FDA), USA
[k] European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC), Belgium

ARTICLE INFO

Keywords:
Regulatory toxicology
Normalisation of 'omics data
Statistical analysis
Differentially expressed genes
Reproducibility
Bioinformatics
Gene expression

ABSTRACT

A generic Transcriptomics Reporting Framework (TRF) is presented that lists parameters that should be reported in 'omics studies used in a regulatory context. The TRF encompasses the processes from transcriptome profiling from data generation to a processed list of differentially expressed genes (DEGs) ready for interpretation. Included within the TRF is a reference baseline analysis (RBA) that encompasses raw data selection; data normalisation; recognition of outliers; and statistical analysis. The TRF itself does not dictate the methodology for data processing, but deals with what should be reported. Its principles are also applicable to sequencing data and other 'omics. In contrast, the RBA specifies a simple data processing and analysis methodology that is designed to provide a comparison point for other approaches and is exemplified here by a case study. By providing transparency on the steps applied during 'omics data processing and analysis, the TRF will increase confidence in the processing of 'omics data, and regulatory use. Applicability of the TRF is ensured by its simplicity and generality. The TRF can be applied to all types of regulatory 'omics studies, and it can be executed using different commonly available software tools.

Regulatory Toxicology and Pharmacology 91 (2017) S3–S13

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

Applying 'omics technologies in chemicals risk assessment: Report of an ECETOC workshop

Roland Buesen [a], Brian N. Chorley [b], Beatriz da Silva Lima [c], George Daston [d], Lize Deferme [e], Timothy Ebbels [f], Timothy W. Gant [g], Amber Goetz [h], John Greally [i], Laura Gribaldo [j], Jörg Hackermüller [k], Bruno Hubesch [l], Danyel Jennen [m], Kamin Johnson [n], Jun Kanno [o], Hans-Martin Kauffmann [a], Madeleine Laffont [p], Patrick McMullen [q], Richard Meehan [r], Mark Pemberton [s], Stefania Perdichizzi [t], Aldert H. Piersma [u, v], Ursula G. Sauer [w], Kerstin Schmidt [x], Hervé Seitz [y], Kayo Sumida [z], Knut E. Tollefsen [aa], Weida Tong [ab], Tewes Tralau [ac], Ben van Ravenzwaay [a], Ralf J.M. Weber [ad], Andrew Worth [j], Carole Yauk [ae], Alan Poole [p, *]

[a] BASF SE, Germany
[b] U.S. Environmental Protection Agency, USA
[c] iMED.Ulisboa and Faculty of Pharmacy, Universidade de Lisboa, Portugal
[d] Procter and Gamble, USA
[e] ExxonMobil Petroleum and Chemical, Belgium
[f] Computational and Systems Medicine, Department of Surgery and Cancer, Imperial College London, United Kingdom
[g] Centre for Radiation, Chemical and Environmental Hazards (CRCE), Harwell Science and Innovation Campus, Public Health England (PHE), United Kingdom
[h] Syngenta Crop Protection LLC, USA
[i] Albert Einstein College of Medicine, Yeshiva University, USA
[j] European Commission, Joint Research Centre, European Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM), Italy
[k] Department of Molecular Systems Biology, Helmholtz Centre for Environmental Research - UFZ, Germany

2016 - Madrid workshop to OECD projects

Reporting templates

Omics reporting framework reporting template

Approved and declassified in November 2023 - For use

Learn more

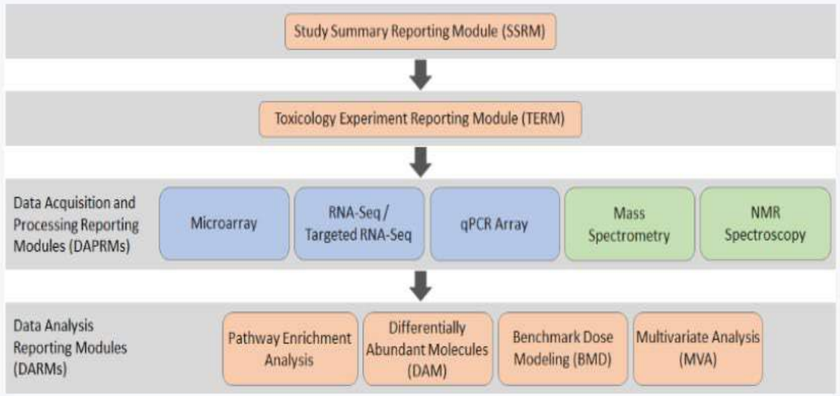
Omics reporting framework reporting template 2022

Draft published in November 2022 - Not for use
(Available only for versioning purposes)

Learn more

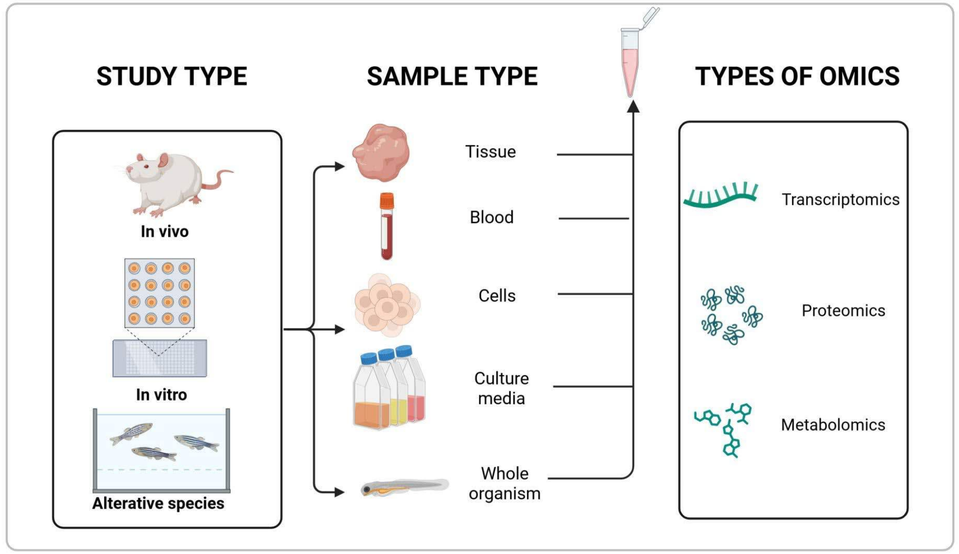
The Transcriptomics Reporting Framework (TRF) and Metabolomics Reporting Framework (MRF) were developed by international teams of experts from government agencies, regulatory bodies, industry and academia. In addition, developing reporting templates and supporting guidance for completing templates, the experts also tested the frameworks in a variety of scenarios.

More information can be found in the publication: *Progress towards an OECD reporting framework for transcriptomics and metabolomics in regulatory toxicology*.



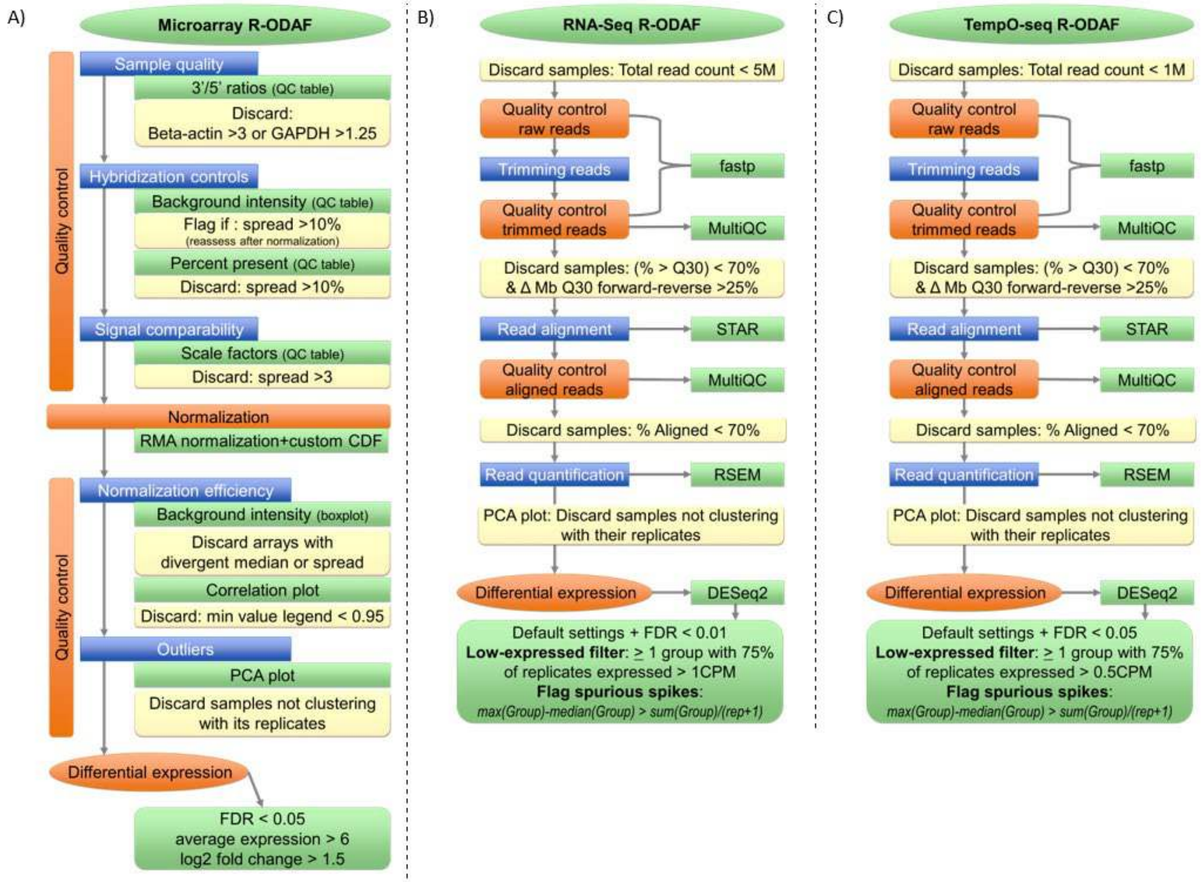
OECD Omics Reporting Framework (OORF)

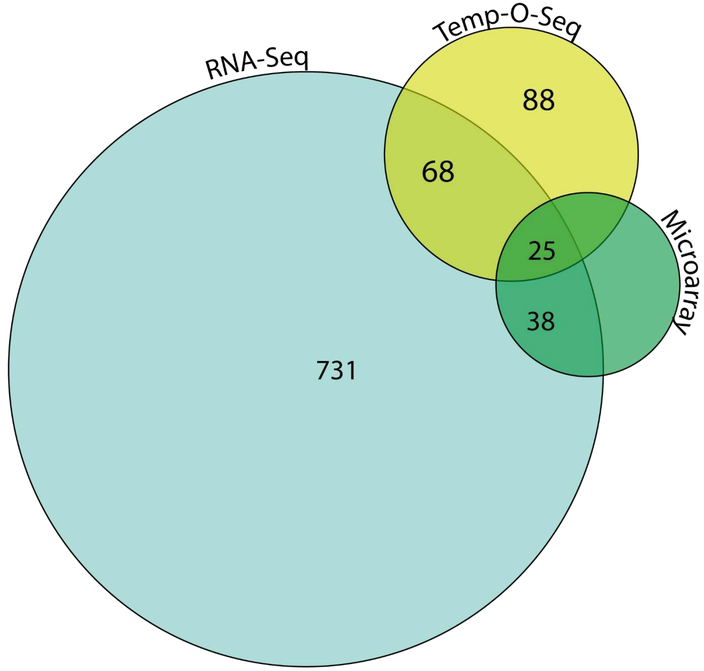
Guidance Document on Good Practices and Standardisation of Sample Collection for Omics Analysis.



CEFIC-LRI C4 output – T ROAM (ODAF – Omics Data Analysis Framework)

Transcriptomics Reference Omics Analysis Method (T-ROAM)





- Adopted as an appendix to the OORF
- Now in the commenting round

2022 – Brussels on-line ☹

Archives of Toxicology
https://doi.org/10.1007/s00204-023-03522-3

MEETING REPORTS

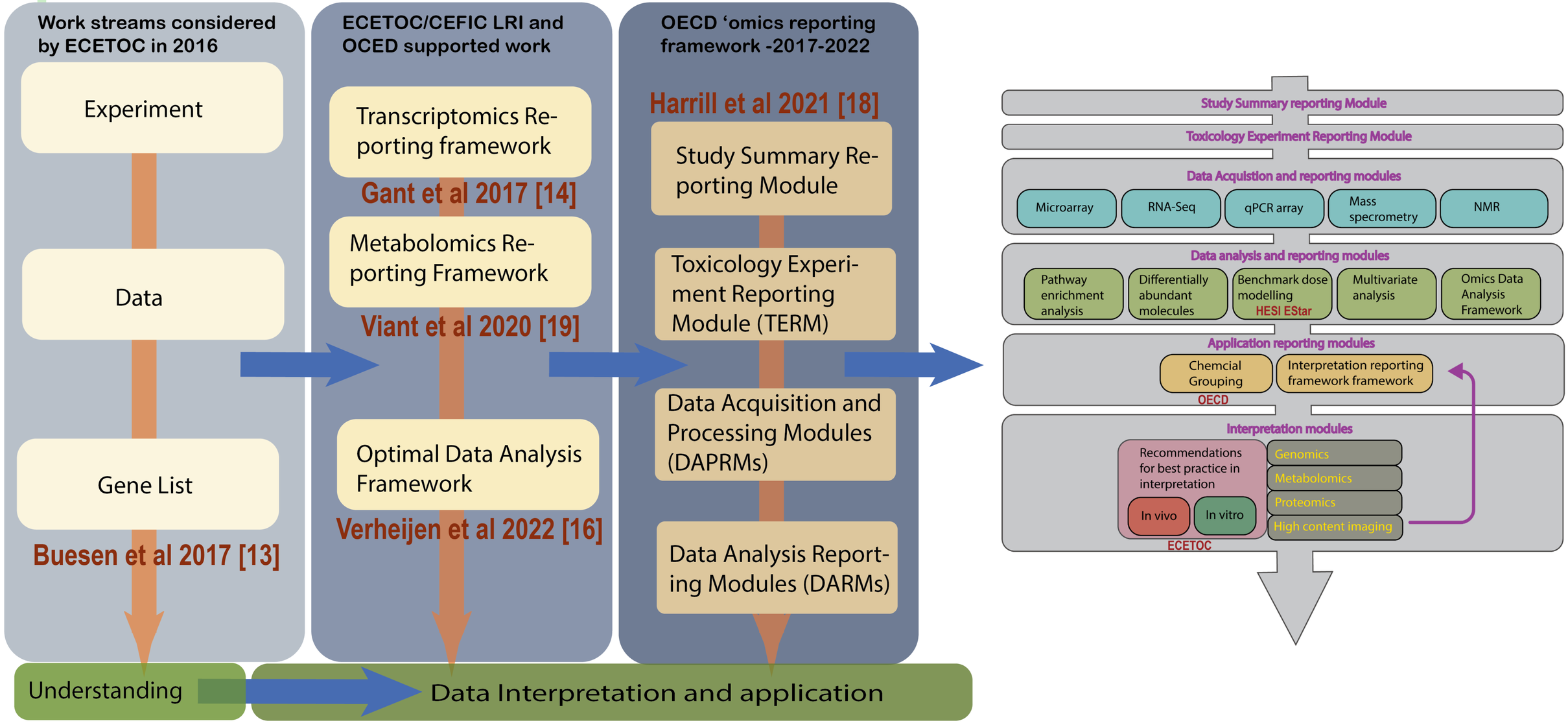
Check for updates

Applying genomics in regulatory toxicology: a report of the ECETOC workshop on omics threshold on non-adversity

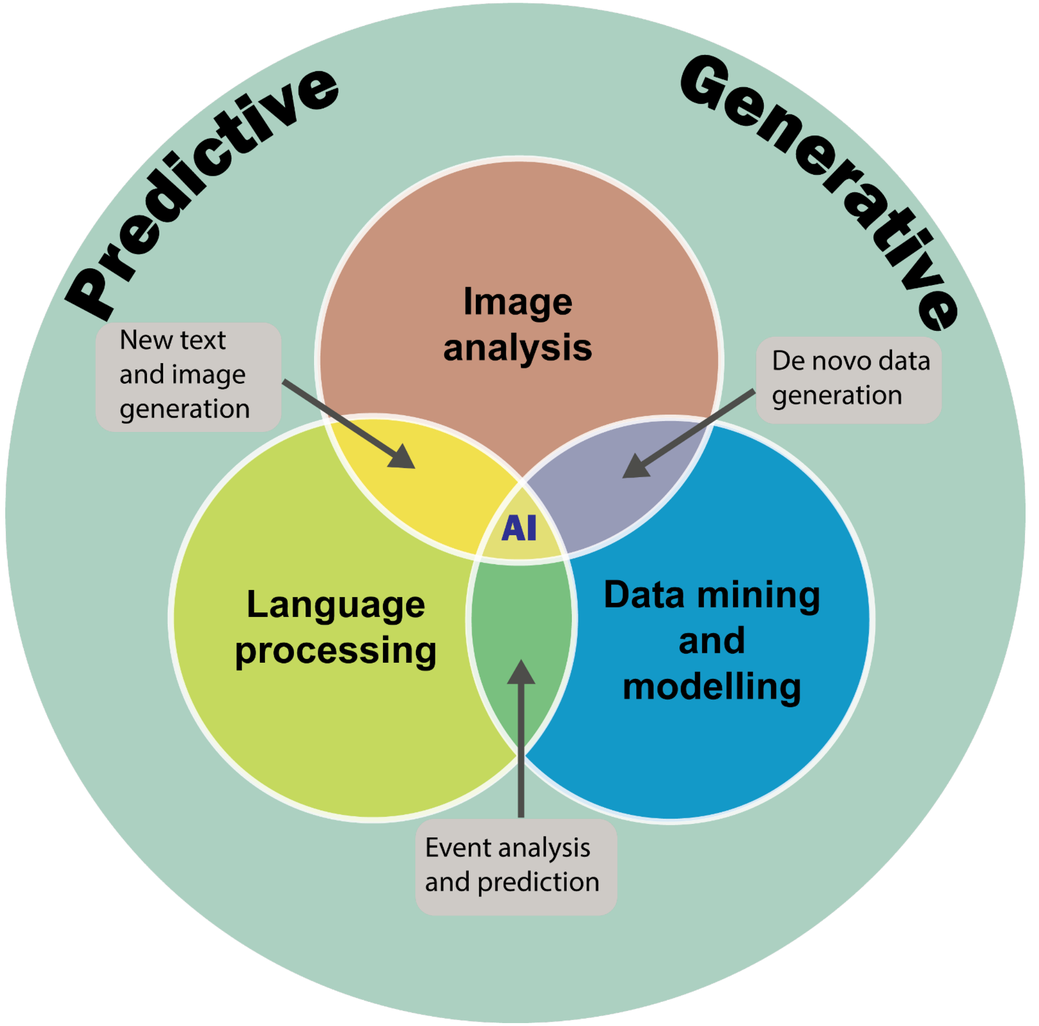
Timothy W. Gant[1,2] · Scott S. Auerbach[3] · Martin Von Bergen[4] · Mounir Bouhifd[5] · Philip A. Botham[6] · Florian Caiment[7] · Richard A. Currie[6] · Joshua Harrill[8] · Kamin Johnson[9] · Dongying Li[10] · David Rouquie[11] · Ben van Ravenzwaay[12] · Frank Sistare[13] · Tewes Tralau[14] · Mark R. Viant[15] · Jan Willem van de Laan[16] · Carole Yauk[17]

Received: 23 January 2023 / Accepted: 11 May 2023

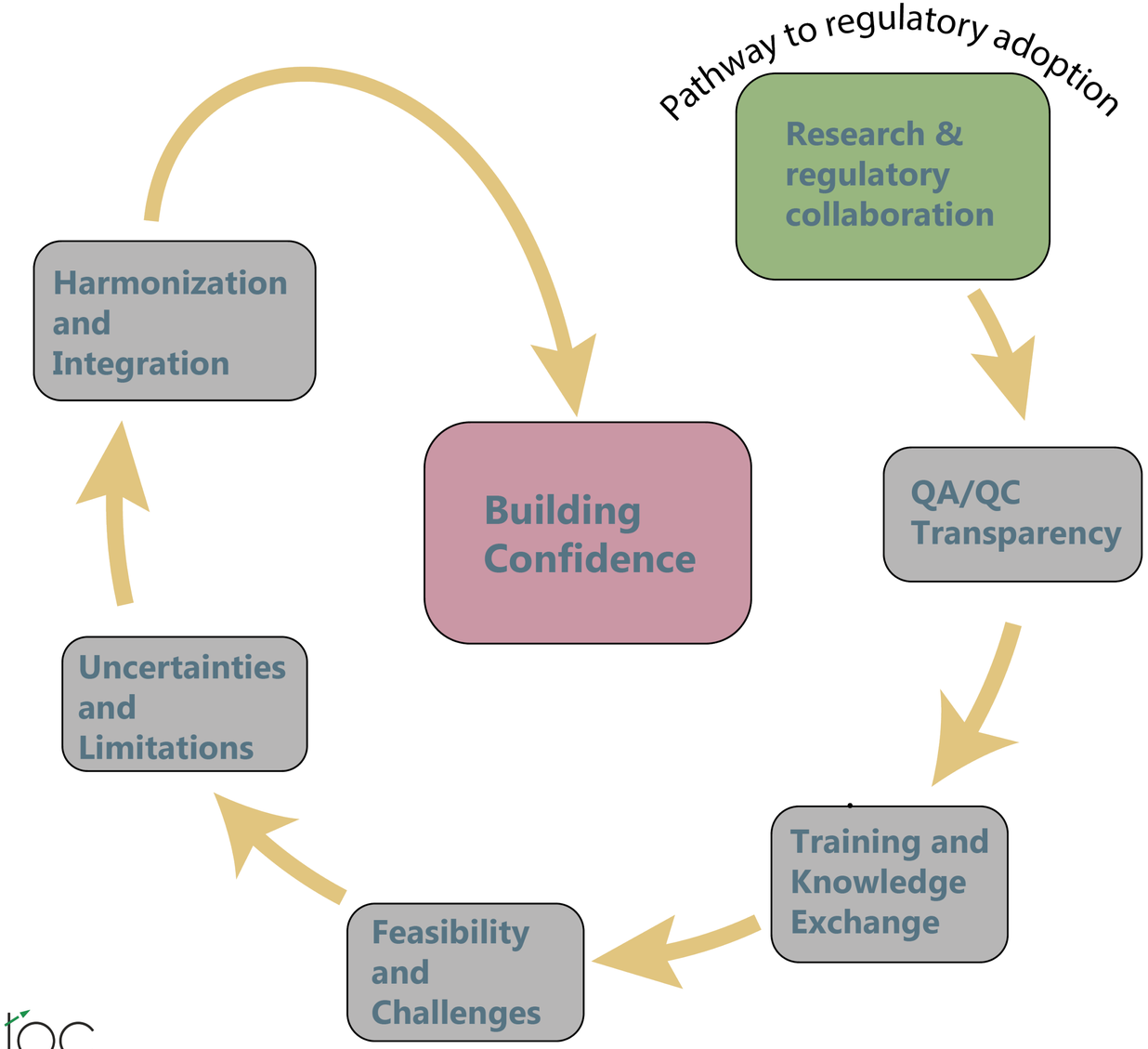
From Madrid to Brussels and on to Paris



2024 – AI and chemical risk assessment : Sophia Antipolis



In conclusion – 2022



- **Thanks to ECETOC for sticking with the pursuit of the pathway for more than a decade – and supporting the hotels in Malaga.**

Some final thoughts from the early days

“The methods that are used to analyze the data can have a profound influence on the interpretation of the results.”

John Quackenbush – 2001 Nature Reviews Genetics

‘…the new technologies impose a greater demand on toxicologists to exercise expert judgement on the meaning of their data….’

Lewis L. Smith – Tips June 2001

Gene expression may identify a hazard, but an assessment of risk requires dose response data, and mechanistic understanding by pathway analysis, particularly at low dose.

Rusty Thomas, George Daston, Heidrun Ellinger-Ziegelbauer - 2008

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

Thank you.

ecetoc
We are the Centre for chemical safety assessment