Occupational Health Clinics for Ontario Workers

Centre de santé des travailleurs et travailleuses de l'Ontario

Causation of Chronic Diseases including Cancer

Dr. Noel Kerin, MD,MSC,FCBOM,CIME

October 30, 2014

Lets Have a Tour!!!

OHCOW 25th Anniversary

- The Past
- The Present
- The Future

The Past

Thank you to the brave men and women who fought for and forged the Ontario Health and Safety Act 1978 and congratulations on your first born in 1989 – the OHCOW Clinics!

OHCOW is at the Coalface

The Present - Confrontational

Nobody wants to accept our causation arguments!

Ask the Advocates in the room!

Why?

Anatomy of a WSIB Case

1. JEM/TEM (Job/Task Exposure Matrix)

2. Occ. Medical/IH/Ergo Opinion + peer reviewed science evidence

3. Advocacy

Chronic Disease Causation

"Current evidence suggests that non-genetic factors contribute about **90%** of the risks of chronic diseases, we have not explored the vast majority of human exposures that might initiate disease processes" (Lichtenstein 2000, Rappaport 2011).

Toxic chemicals enter the body not only from:

- exogenous sources (air, water, diet, drugs, and radiation) but also from:

- endogenous processes, including inflammation, lipid peroxidation, oxidative stress, existing diseases, infections, and gut flora.

The Future - Challenges for OHCOW

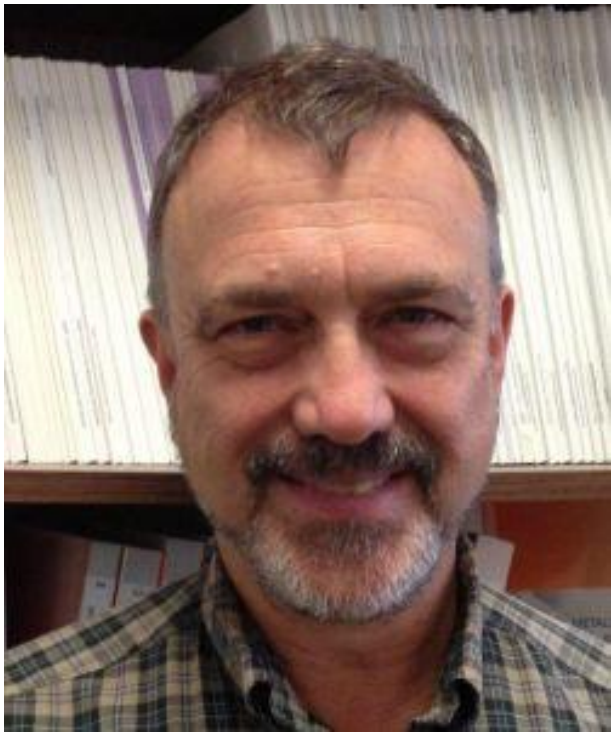
Limited historical and present personal worker exposure data!

- How do we get reliable exposure data?
- How do we use it?

The Future

- Human Genome Sequencing – 2003
- Exposome – 2005 (C. Wild, IARC, 2005)
- Genetic Finger Printing – 2010 (C. McHale, Berkley)

Occupational Cancer Research Centre - OCRC



OCRC is the first of its kind in Canada, and was created to bridge the gaps in our knowledge of occupation-related cancers and to translate these findings into preventive programs to control workplace exposures and improve the health of Ontarians.

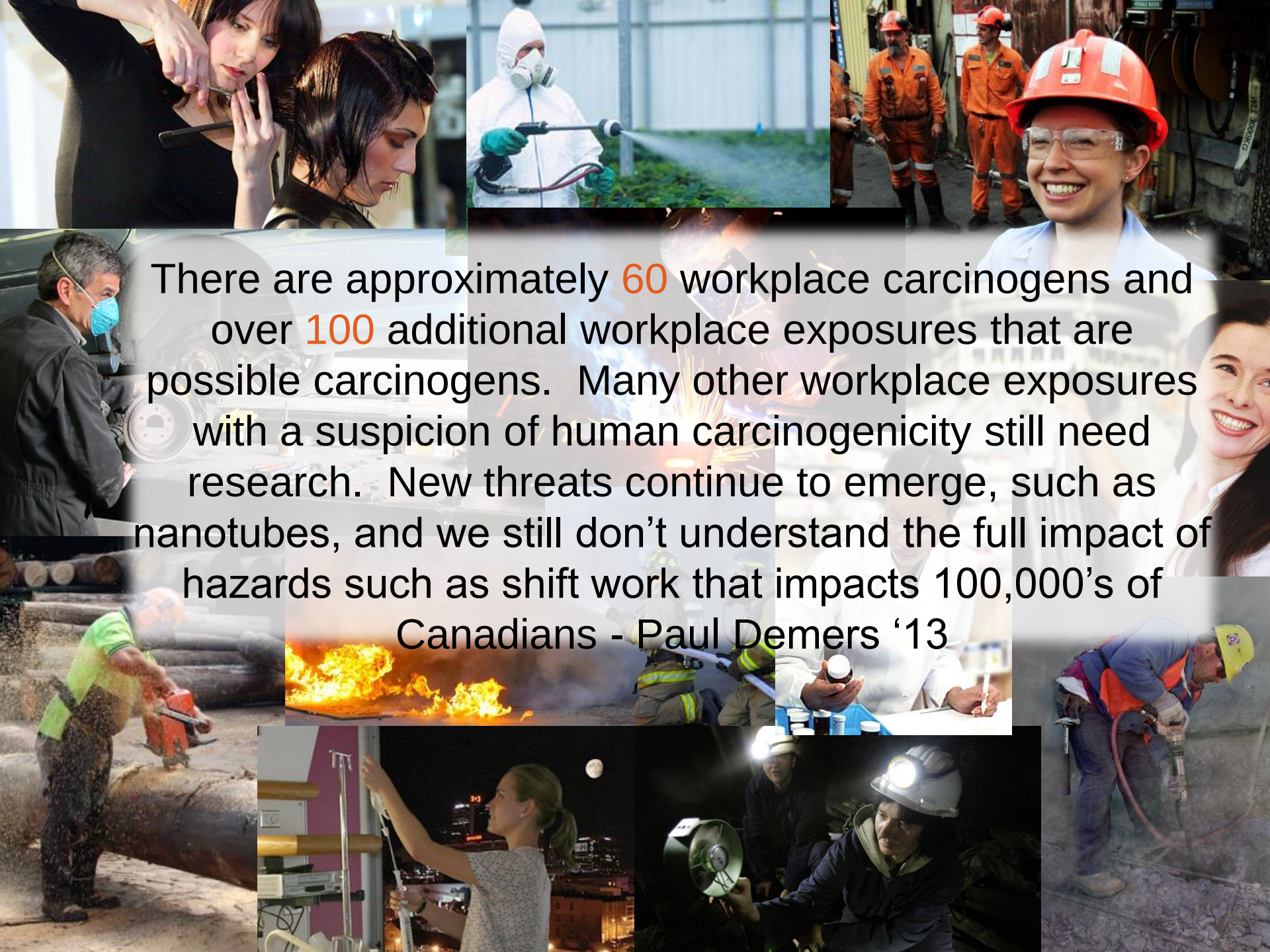
Dr. Paul Demers, Director

25th Greetings from Dr. Demers

"Hello to OHCOW and your audience.

Happy 25th Anniversary – keep up the great work!"

"The following are some of my thoughts on the future challenges dealing with occupational diseases."



There are approximately 60 workplace carcinogens and over 100 additional workplace exposures that are possible carcinogens. Many other workplace exposures with a suspicion of human carcinogenicity still need research. New threats continue to emerge, such as nanotubes, and we still don't understand the full impact of hazards such as shift work that impacts 100,000's of Canadians - Paul Demers '13

Did a 30 year chemical and dust exposure history cause **PROSTATE** cancer – 59 yr old ♂?

19 carcinogenic risk factors identified

- Asbestos
- Arsenic
- Aromatic Amines (*n*-Nitrosamines)
- Benzene
- Cadmium
- Cigarette smoking
- Dioxins
- Endocrine disruptors (Bisphenol A – Epoxy constituent (BPA)
- Formaldehyde
- Lead
- Metal Working Fluids
- Polycyclic Aromatic Hydrocarbons (PAHs)
- Polyvinyl chloride (PVC)
- Shiftwork
- Rubber curing chemicals
- Quartz Silica
- Trichloroethylene (TCE)
- Diesel exhaust fumes
- Chromium VI

Chronic Myeloid Leukemia (CML) – 49 yrs male

Diagnoses

1. CML
2. Chloracne
3. Ch.Tox.Encephalopathy
4. Peripheral Neuropathy
5. GERD
6. Brain Aneurysm

Exposures

- PAHs
- PVC
- Solvents
- Formaldehyde
- Cadmium
- Glues
- Pigments
- Welding Fumes
- Quartz Silica

Crop Dusting Spray vortex

Combined Chemical Mixtures

- Multiple chemical exposures can have antagonistic, additive, if not multiple or synergistic effects one on the other.

- Chemical mixtures in formulations may thus be underestimated regarding their toxic or hormonal impact.

NIOSH (NORA) - 2004

E. Monosson - 2005

EU-ULSOP - State of the Art Report on Mixture Toxicity - 2009

Professor David Goldsmith – Geo.Washington Univ.

The Silica Story as told by Dr. Goldsmith – a founding father of silica toxicity and the epidemiology of silica cancer causation

Video

What is the Exposome?

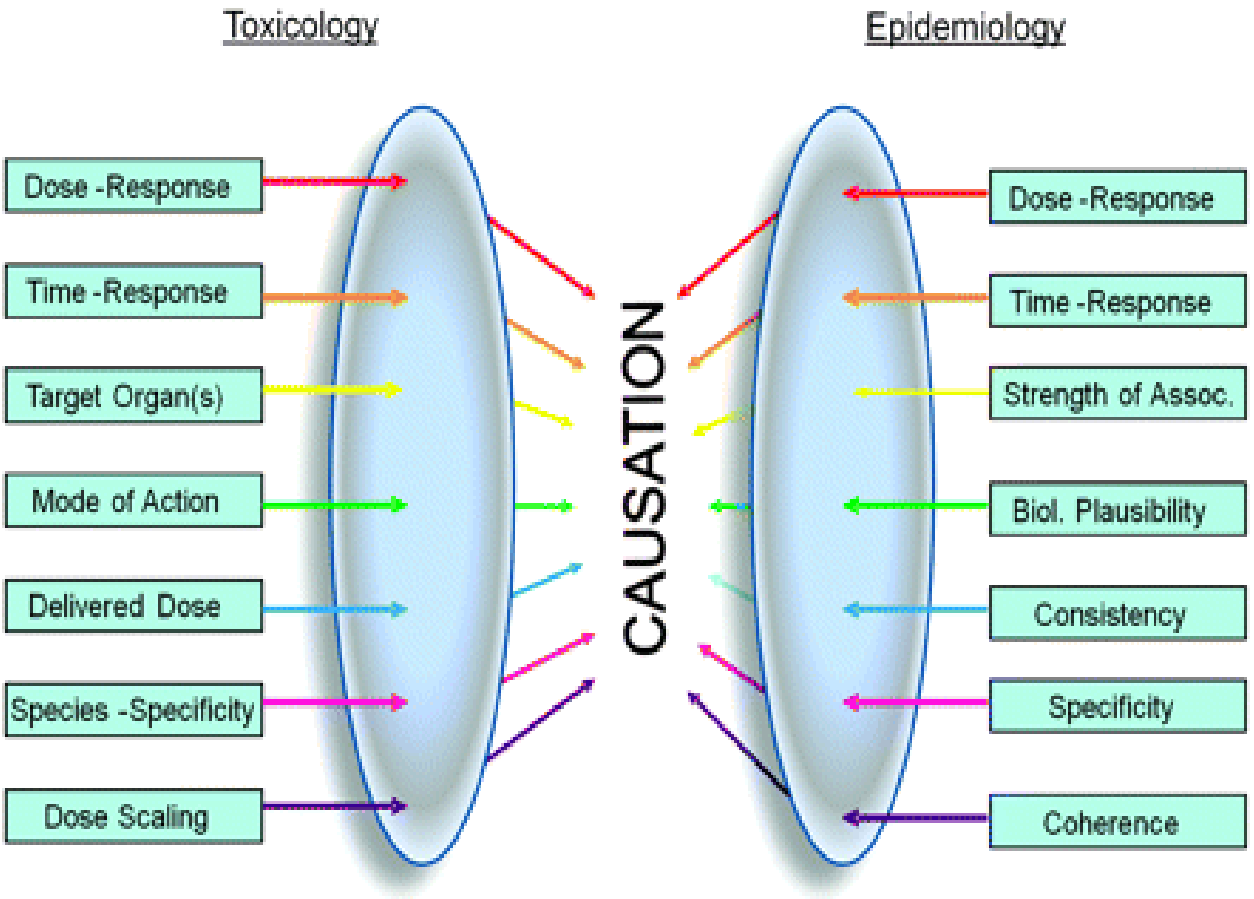
Success in mapping the human genome has fostered the complementary concept of the "Exposome“ (Wild, IARC,2005).

The Exposome can be defined as: “the measure of all the exposures of an individual in a lifetime and how those exposures relate to health”.

An individual’s exposure begins before birth and includes insults from environmental and occupational sources.

Understanding how exposures from our environment, diet, lifestyle, etc. interact with our own unique characteristics such as genetics, physiology, and epigenetics impact our health is how the Exposome will be articulated.

Toxicology .v. Epidemiology



Hans-Olov Adami et al., 2011

Exposome - New Tools & Technologies

Exposome can be applied to address these challenges and include:

- exposure biomarker technologies
- high-throughput molecular 'omics' laboratory techniques.
- geographical mapping
- remote sensing technologies,
- smartphone applications (apps)
- personal exposure sensors

Exposome - Benefits to Epidemiological Research

(1) accurate and reliable measurement of many exposures in the external environment

(2) the measurement of a wide range of biological responses in the internal environment

(3) addressing the dynamic, life course nature of the Exposome.

Exposome - Benefits to Epidemiological Research (cont.)

- Prospective, population-based cohort studies have recently started to implement these methods using the exposome framework.
- The exposome thus offers a new and exciting paradigm for improvement and integration of currently scattered and uncertain data on the environmental component in disease aetiology.

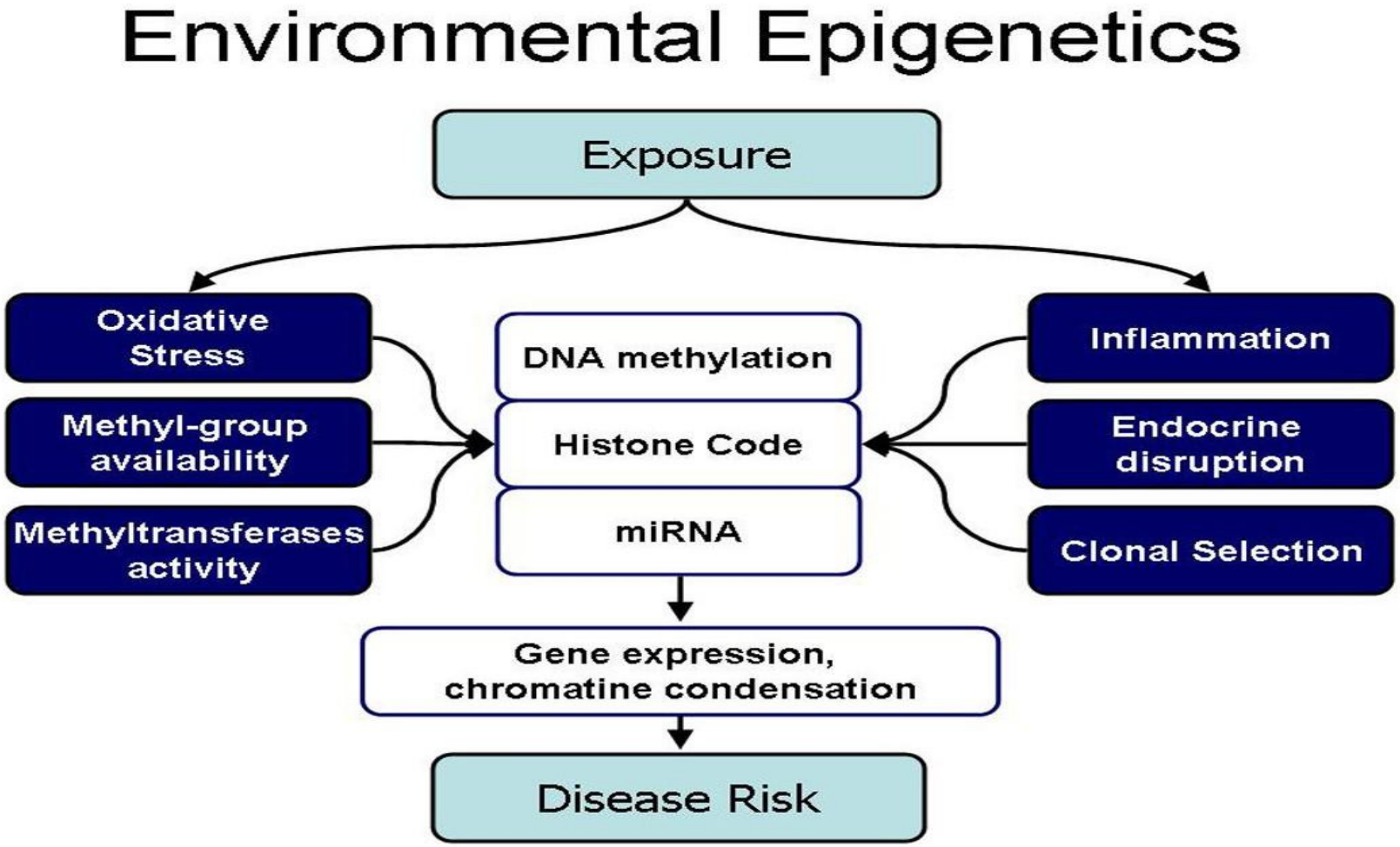


Figure 1. Potential mechanisms linking environmental exposures to epigenetic effects Environmental chemicals may modify multiple biological processes that affect epigenetic mechanisms, including DNA methylation, histone codes, and miRNA expression. These changes may, in turn, modify chromatin organization and condensation, gene expression, and affect disease risk.

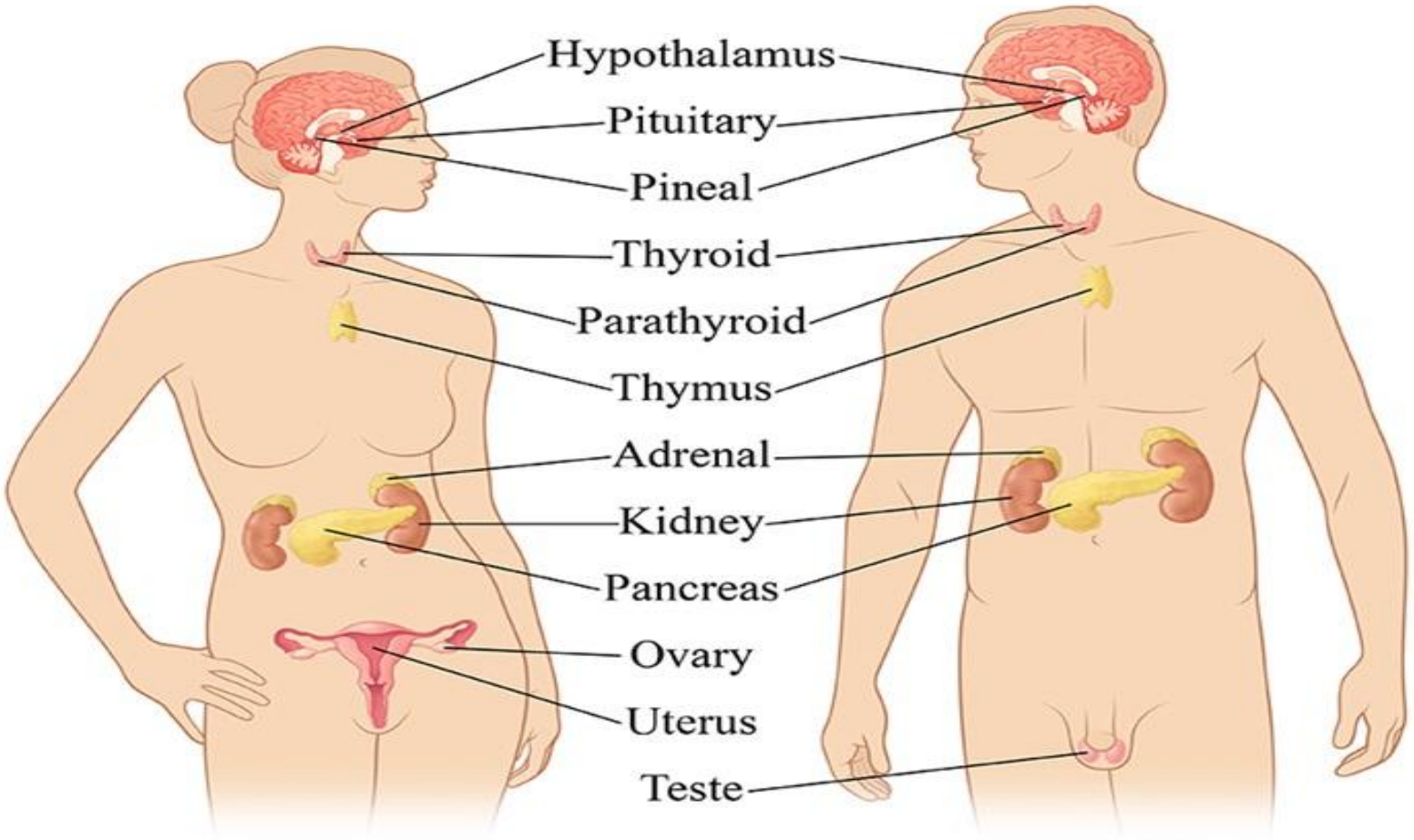
The preceding slide “Environment Epigenetics” is taken from : Baccarelli, Andrea, and Valentina Bollati. "Epigenetics and environmental chemicals." Current opinion in pediatrics 21.2 (2009): 243

Endocrine Disruption Chemicals (EDCs) & EDCs Contribute to the Development of Health Problems

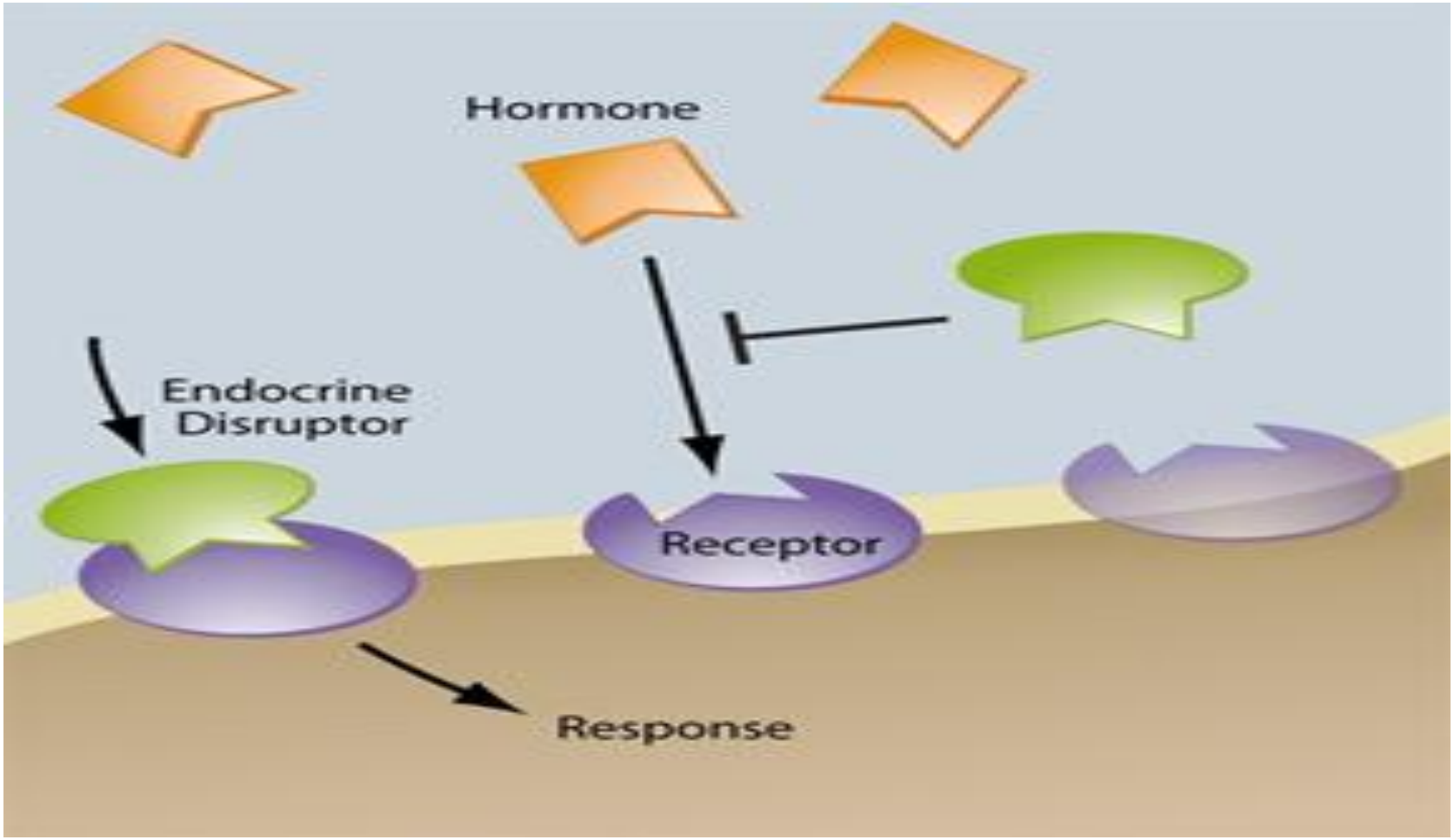
- Breast cancer in women
- Prostate cancer in men
- Thyroid cancer
- Obesity
- Diabetes Mellitus
- Non-descended testes in young males
- Developmental effects on the nervous system in children, attention deficit /hyperactivity in children

WHO/UN study, 2013

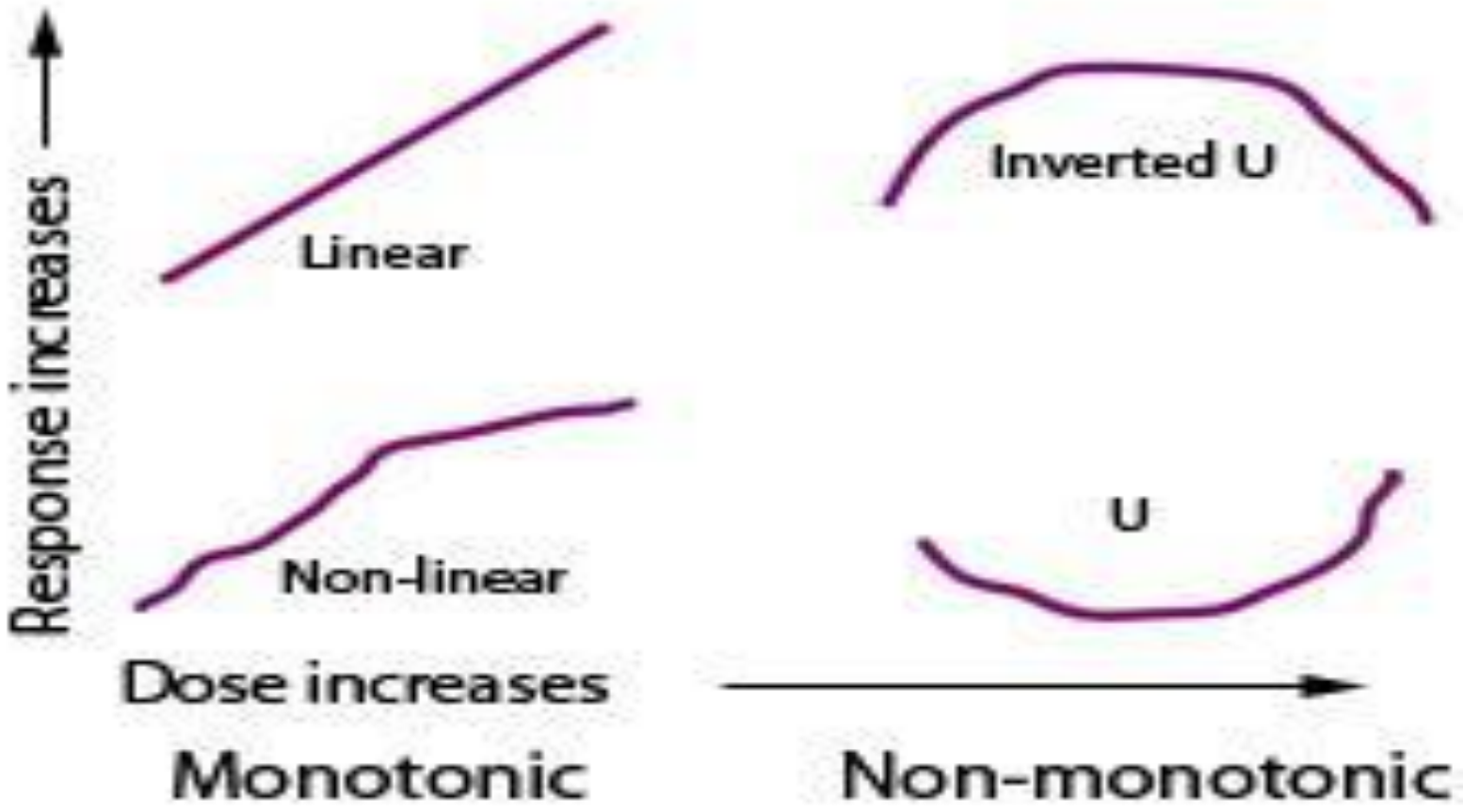
EDCs - What's Missing?



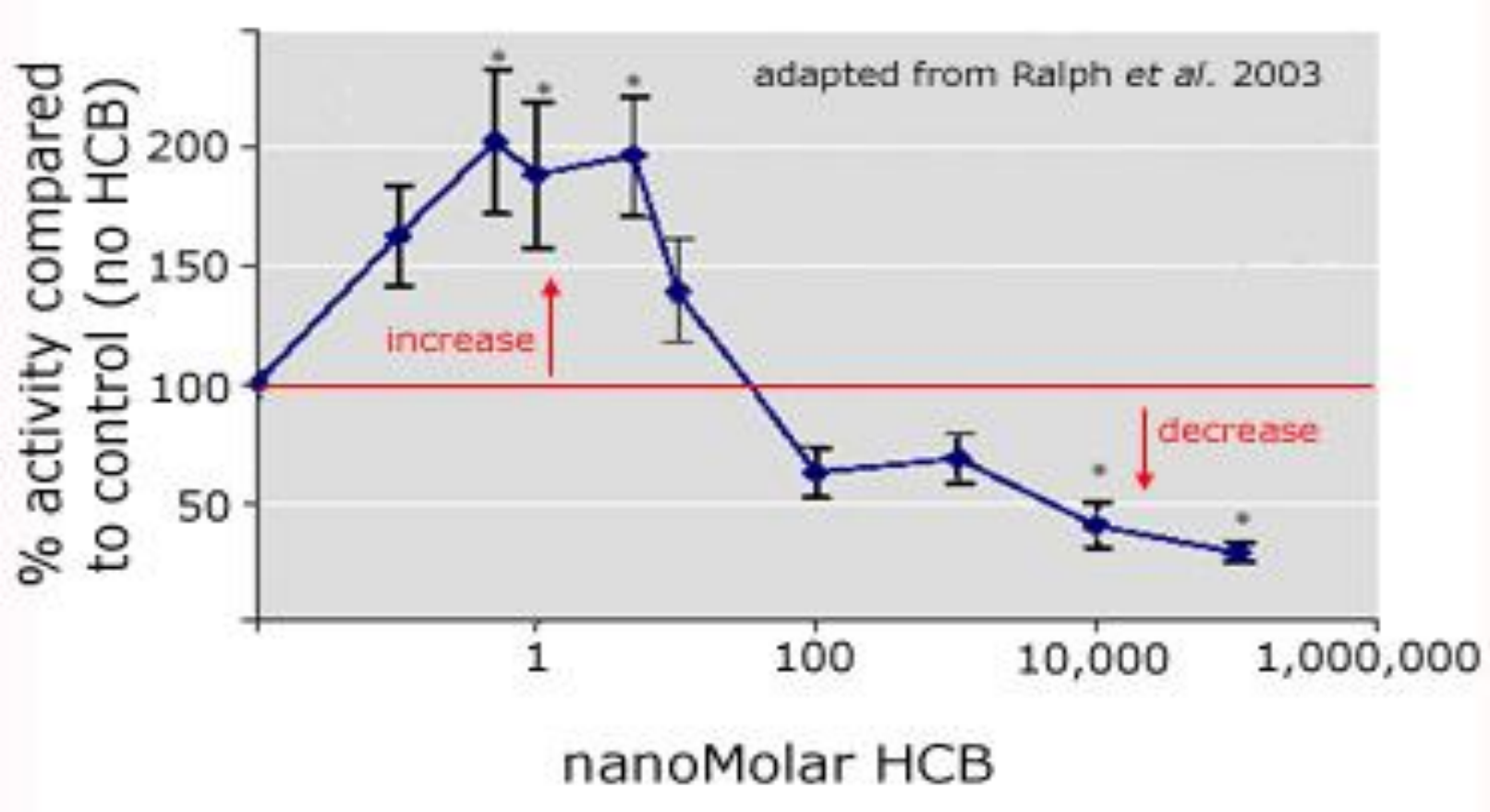
EDCs – How They Act



Monotonic/Non-Monotonic Response



Non-Monotonic Dose Response



EDCs

"We urgently need more research to obtain a fuller picture of the health and environment impacts of endocrine disruptors"

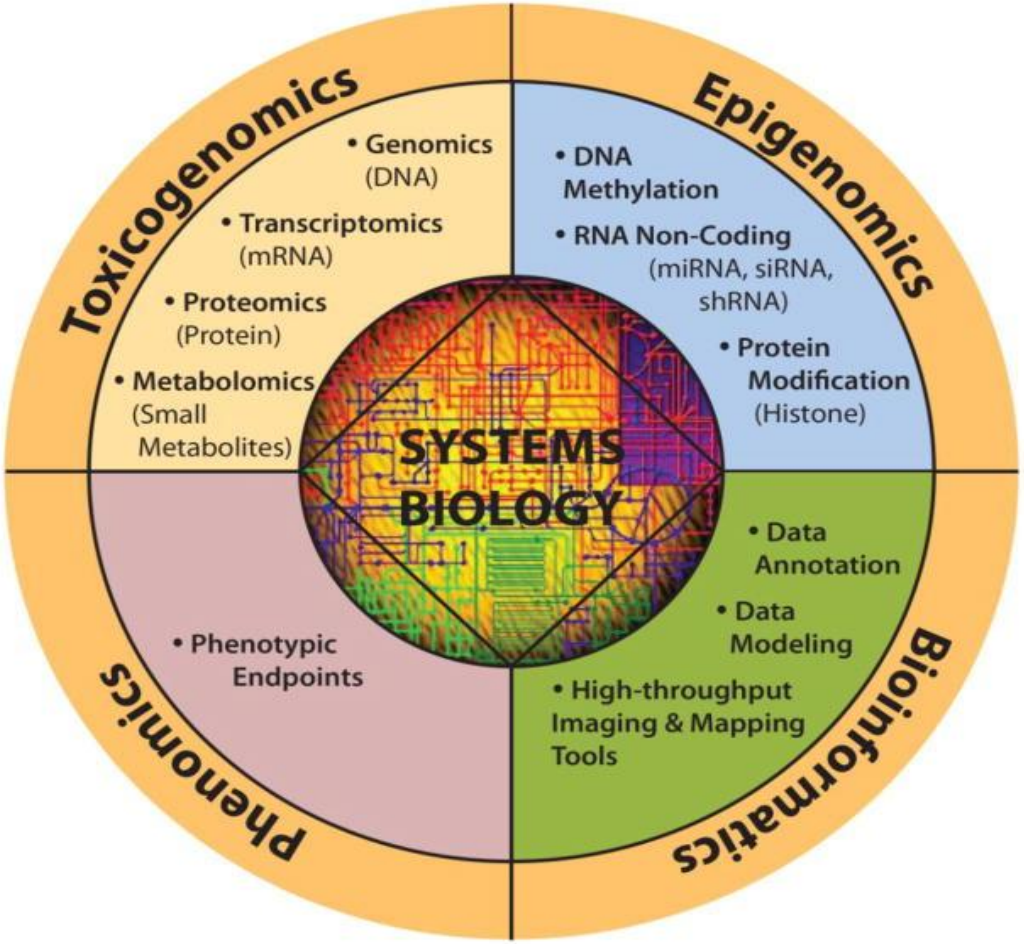
Dr. Maria Neira, WHO's Director for Public Health and Environment
Feb. 2013

Systems Biology

- systems biology is a recent and evolving interdisciplinary field that focuses on the systematic study of complex interactions in biological systems.
- employs a holistic approach to study all components and interactions in the network of DNA (genes), RNA, proteins and biochemical reactions within a cell or organism

McHale et al.,2010

Overview of systems biology and its components



Next Generation Risk Assessment (NexGen)

- NexGen is a multiyear, multi-organization effort to evaluate use of:
- molecular,
- computational, and
- systems biology to better inform risk assessment.

The goal is to advance risk assessment by facilitating faster, less expensive, and more robust assessments of public health risks.

EPA, 2013

“Omic” Technologies

“Together, these omic technologies can each provide a “molecular signature” or “fingerprint” of chemical exposure, early effect or genetic susceptibility, which may enhance our understanding of gene-environment interactions. Thus, this holistic approach known as systems biology has the potential to comprehensively define the mechanisms contributing to disease.”

Zhang, L. et al 2010, UC, Berkley

“Intrinsic Tumor Suppression”

Professor Gerard Evan, Genetic Oncologist

Cambridge University in England and the University of California-San Francisco

“I began as a cancer researcher in 1977 and for twenty years we were banging our heads on a brick wall. Then in the mid-1990s the field was suddenly transformed as we began to understand molecular processes. It is as if there were libraries all over the world full of books written in a language we did not understand. Now we understand that language.”

“Switchable Genetic” Technologies

Our laboratory is developing a suite of “switchable genetic” technologies that allow the reversible systemic or tissue-specific toggling on and off of any target gene in adult mice.

“I can pretty confidently say that my children will never have to worry about dying from cancer,” he commented. “I’m more worried about global warming than my children dying of cancer.”

G. Evans, 2014

Presentation Summary
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What is The Future for OHCOW?

Audience participation Please!!

Thank you