

# Factors to Consider When Trying To Find A Cause For Cancer

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# Quick Bio

- B.S. Molecular and Cellular Biology
  - University of Illinois in Urbana-Champaign, 2008
- M.S. Molecular Biology, Microbiology, and Biochemistry
  - Southern Illinois University, 2010
- Research Technician
  - Arizona Cancer Center, 2010-2013
- Laboratory Scientist
  - NuvOx Pharma LLC, 2012
- Ph.D. Pharmacology and Toxicology
  - University of Arizona, 2018

# Disclaimer

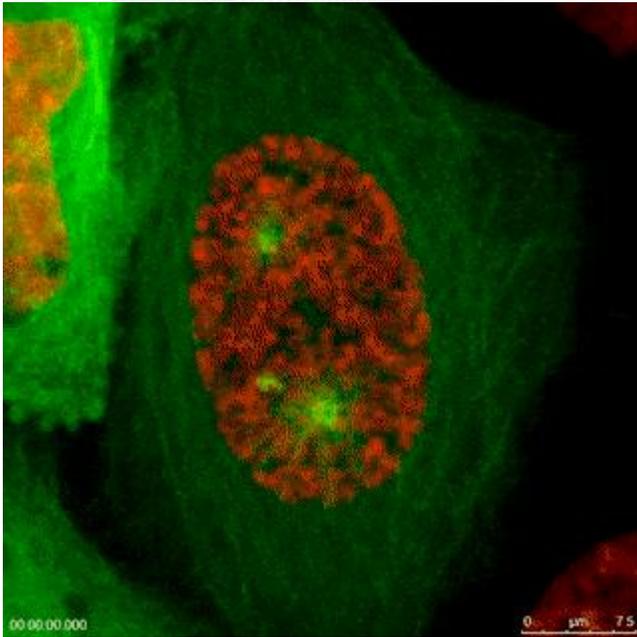
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# Presentation Outline

- Background: Cancer, Carcinogenesis, and Risk Factors
- Resources for Identifying Carcinogens
- Toxicologist Tools for Assessing Causation

# Cancer

A disease in which some of the body's cells grow uncontrollably and spread to other parts of the body



## How cancer starts

Normal cells



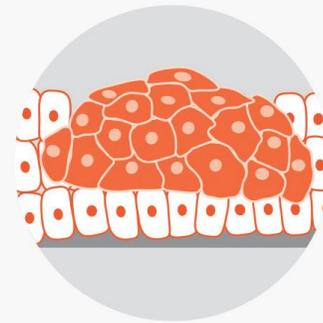
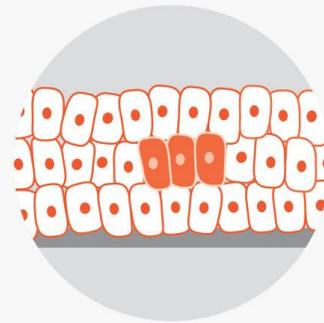
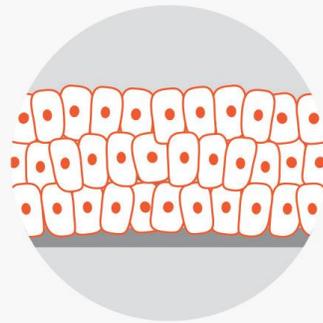
Abnormal cells



Abnormal cells multiply



Malignant cancer

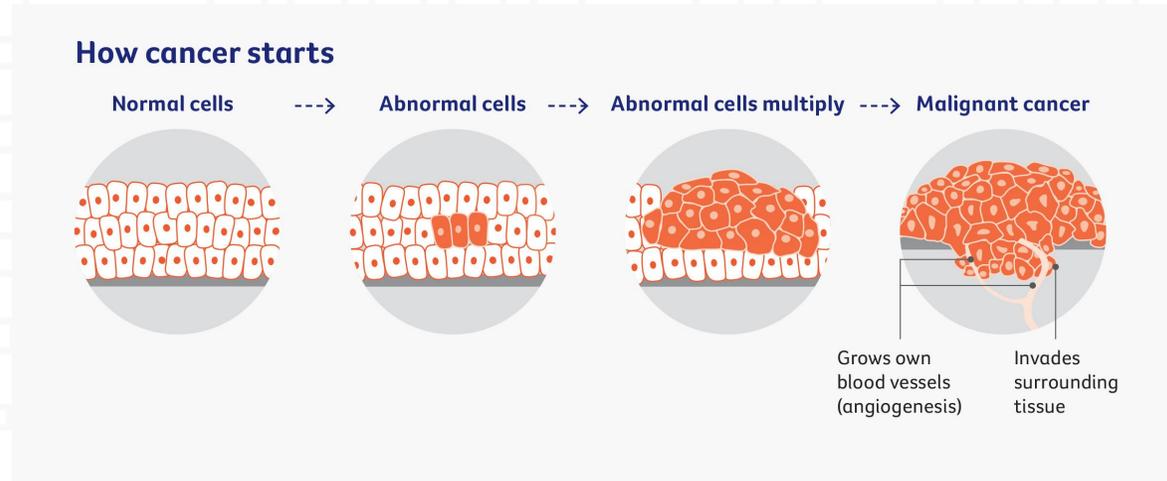


Grows own  
blood vessels  
(angiogenesis)

Invades  
surrounding  
tissue

# Cancer

- Trends in cancer resemble a “de-evolution” (My opinion)
  - Cells no longer act under the control of source tissue or serve the larger organism
  - Behave more like a bacterium
    - Rapidly consume resources
    - Divide and expand population as quickly as possible
    - Attempt to move to new locations for new resources

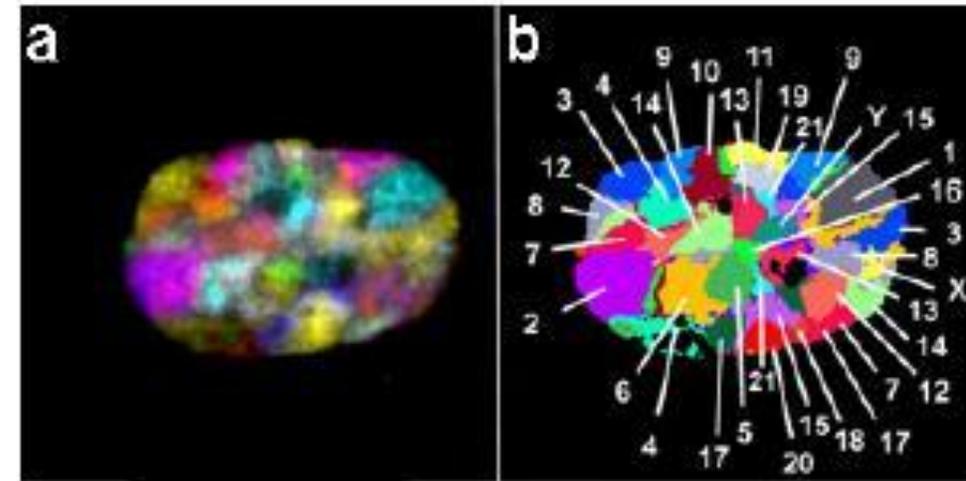
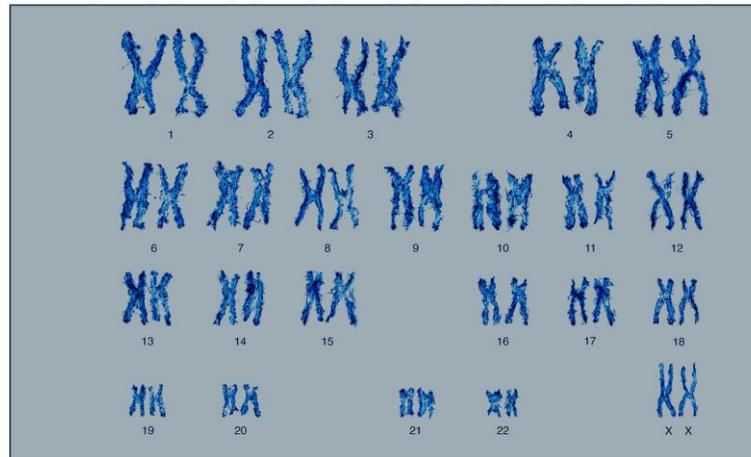
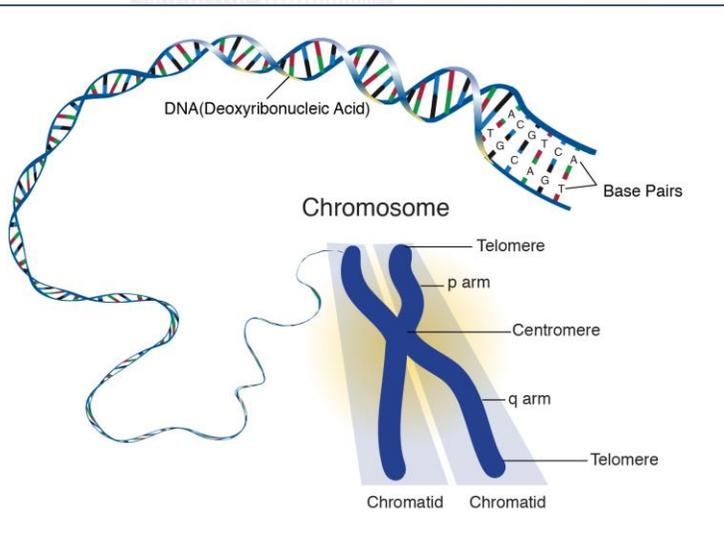
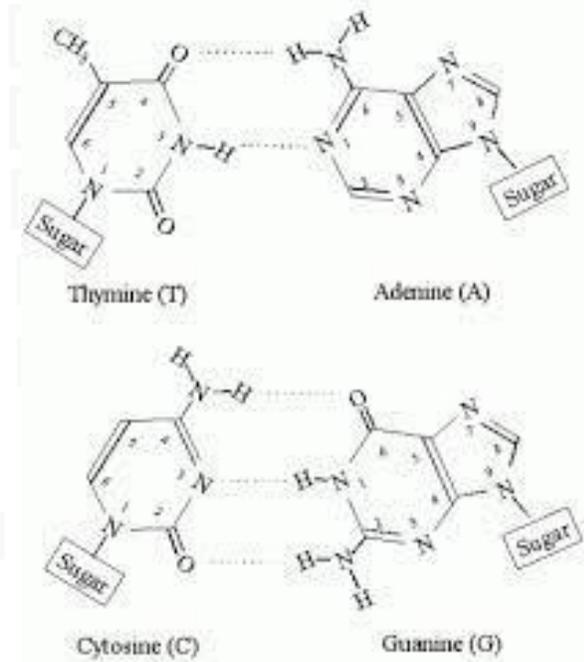


# Cancer/Carcinogenesis

- Cancer is a genetic disease – cause by changes to the genes encoded in our DNA
- Two main ways this occurs (Carcinogenesis = formation of cancer)
  - Genetic Mutation: actual physical changes to the genetic sequence encoded in DNA. Can happen:
    - Naturally when errors in replicating DNA are made by a normally dividing cell
    - DNA damage due to chemical or physical stressors
    - Inherited from our parents
  - Epigenetic Dysregulation: inappropriate changes to how DNA is folded and/or genes are read

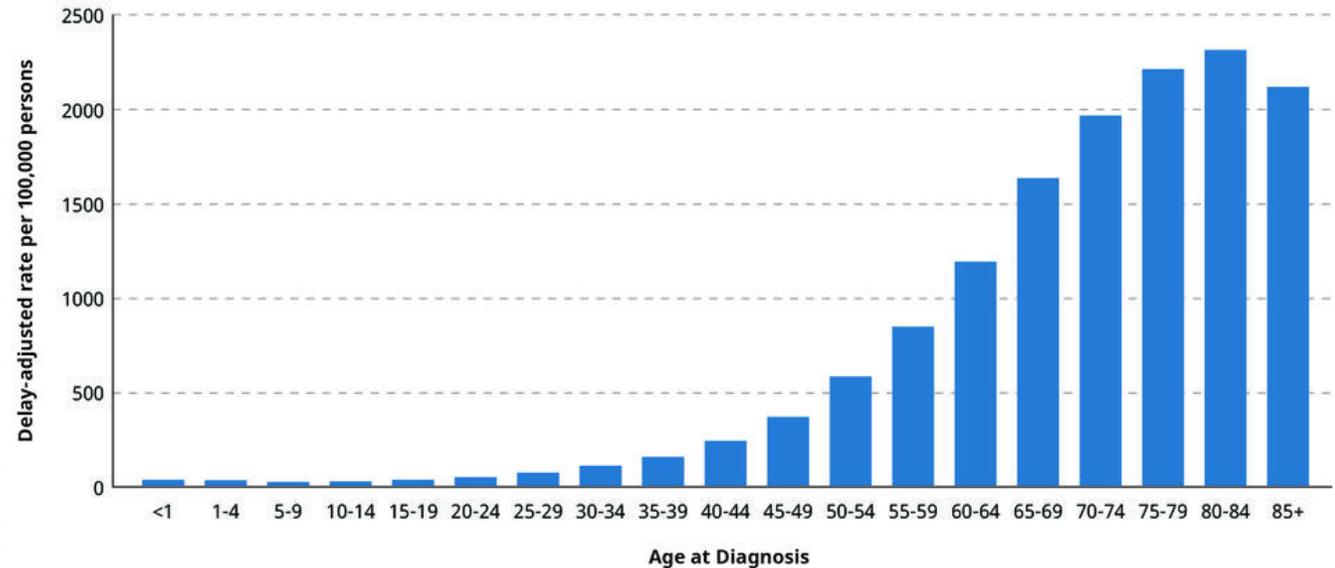
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# Cancer/Carcinogenesis

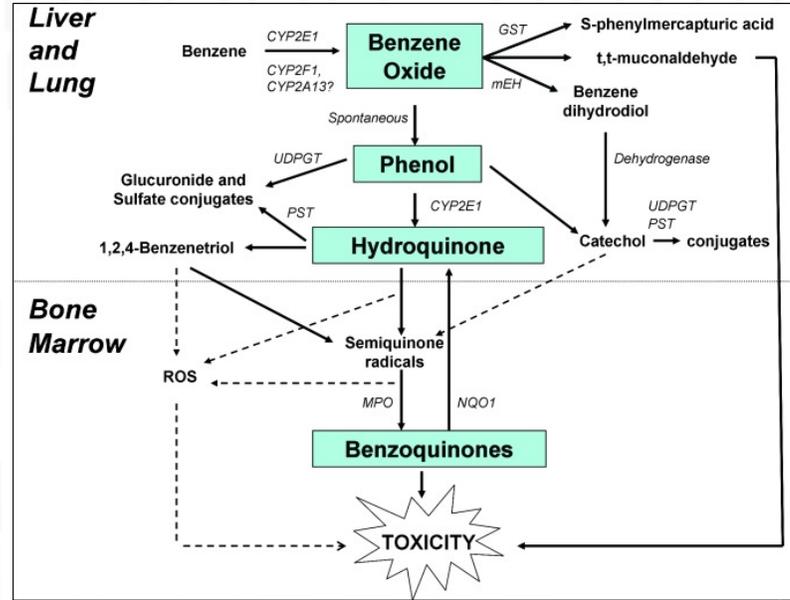
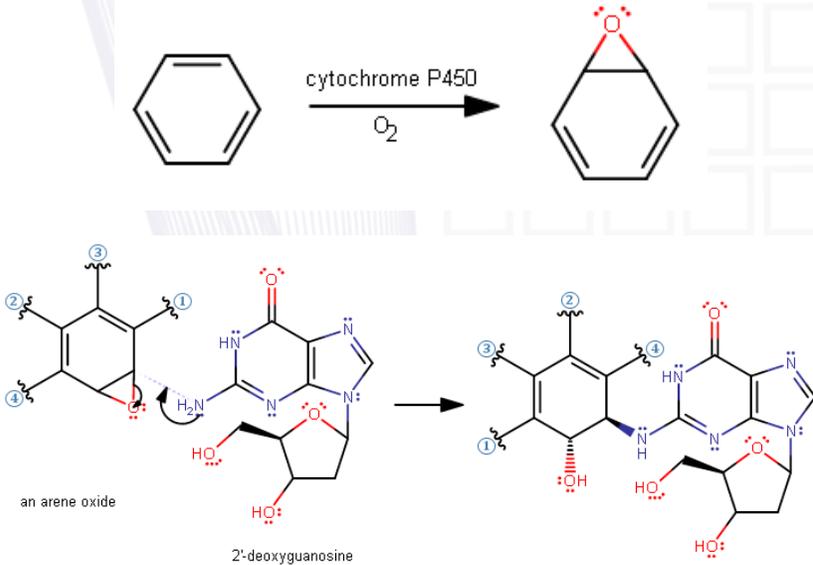
- Most important risk factor for cancer: age
  - Age = more dice rolls on genetic mutation
- Other risk factors
  - Chronic Inflammation
  - Diet
  - Hormones
  - Immunosuppression
  - Infectious Agents
  - Obesity
  - Sunlight/Radiation
  - Alcohol/Tobacco/Cancer-Causing Substances
- Development of cancer is not new
  - Evidence of osteosarcoma in human ancestor foot bone – 1.7 million years old!
- Development of cancer not limited to humans



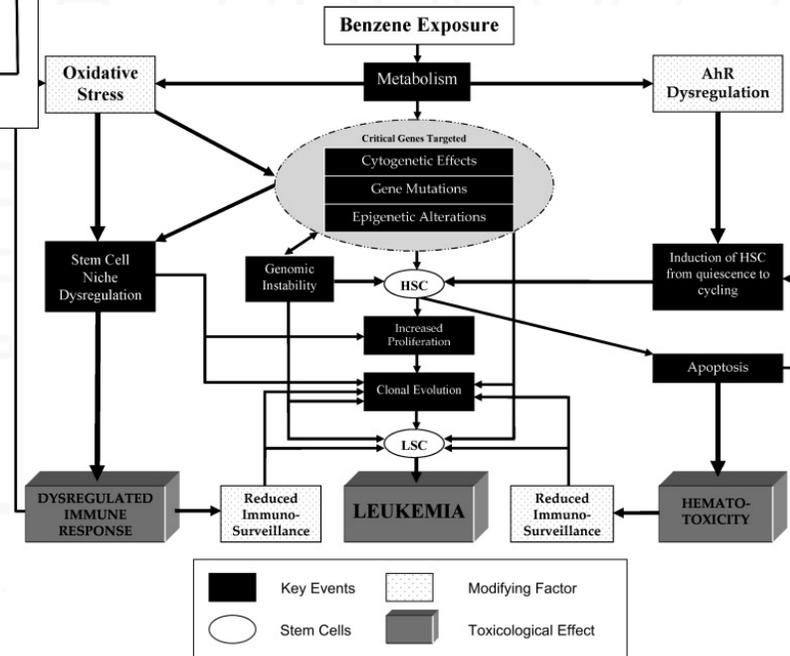
“Civilization did not cause cancer, but by extending human life spans, civilization unveiled it.”  
-Dr. Siddhartha Mukherjee (*The Emperor of All Maladies: A Biography of Cancer*)

# Cancer/Carcinogenesis – Benzene as an Example

Classic Mechanism...



... However, there's way more to it and likely still more we don't know!



# Where Do You Start When Figuring Out A Cause for Cancer?

- Questions to ask:
  - What type of cancer developed?
  - What are the individual's existing risk factors for cancer?
    - e.g. age, diet, general health status, occupation, known exposures, genetic predispositions
  - What is the available evidence that any of the risk factors could have caused the cancer that developed?
    - Where do I find this information???

# Sampling of Some High-Quality Scientific Journals

- New England Journal of Medicine (NEJM)
- Nature (Various Publications)
- Cell
- Science
- Lancet
- Chemical Reviews
- JAMA – Journal of the American Medical Association
- CA (cancer journal from the American Cancer Society)

These journals all have a high barrier to entry and are held in high esteem amongst academic circles. The result is that everyone wants to publish in these journals, and so they often receive the highest quality work.

**Important Note:** There are plenty of high-quality studies/publications in other journals, its just easier to draw a sweeping generalization for these ones.

# General Types of Studies in the Scientific Literature

## Descriptive Research

Includes:

1. Case Studies
2. Observational Research
3. Survey Research

Strengths:

1. Provides in-depth information about a topic
2. Can generate new research questions and hypotheses from details generated
3. Data may be more readily available

Weaknesses:

1. Cannot determine a cause-and-effect relationship from data
2. Can introduce behavior changes if subjects know they are being studied

## Correlational Research

Includes:

1. Epidemiology Studies

Strengths:

1. Can study complex relationships with many variables
2. Allows for making predictions
3. Can determine if two variables are not related
4. Data may be more readily available

Weaknesses:

1. Cannot determine causation even if two variables are related

## Controlled Experimentation

Includes:

1. In Vitro Studies (lab dishes)
2. Animal Studies
3. Human Studies

Strengths:

1. Can determine cause and effect relationships

Weaknesses:

1. Can be time consuming and/or expensive
2. Relevance of in vitro and animal studies to human health not always clear
3. Controls can make experiment less relevant to actual life or may be logistically impossible

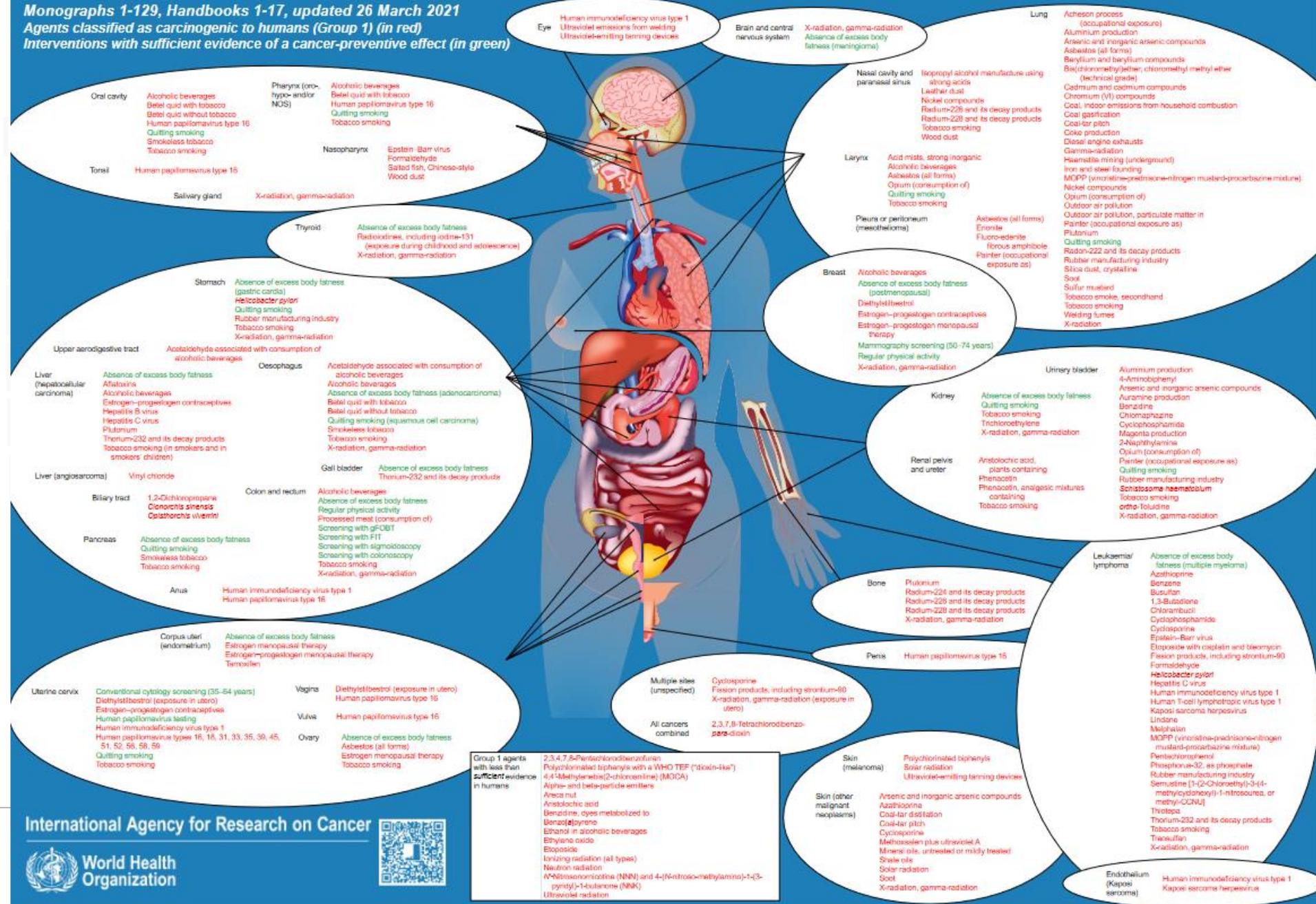
# Authoritative Bodies for Cancer Guidance

- International Agency for Research on Cancer
  - Produce the IARC Monographs – one of the most widely used resources on whether a chemical or substance is considered a carcinogen
- US National Toxicology Program (NTP)
  - Produces the public health document Report on Carcinogens
- Occupational Safety and Health Administration (OSHA)/American Conference of Governmental Hygienists (ACGIH)
  - Produce occupational safety levels = guidelines for chemical concentrations to which workers can be exposed at work with no expected health effects
- Others as well!

# Human Cancer: Known Causes and Prevention by Organ Site

## IARC Monographs on the Identification of Carcinogenic Hazards to Humans and Handbooks of Cancer Prevention

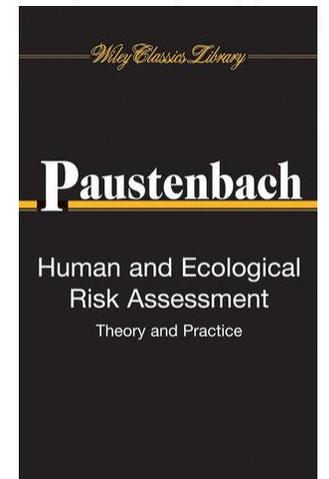
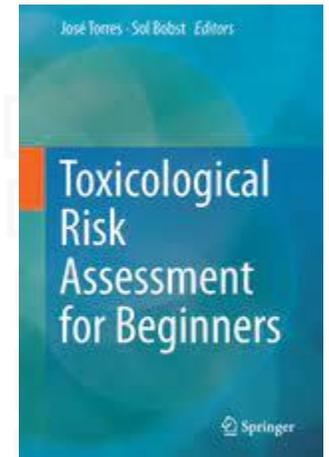
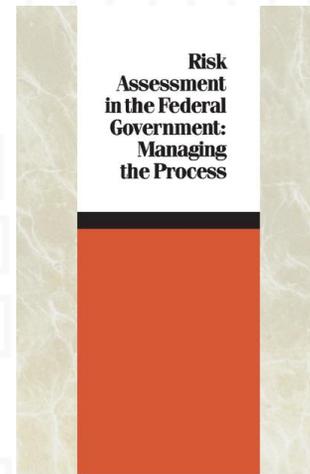
Monographs 1-129, Handbooks 1-17, updated 26 March 2021  
 Agents classified as carcinogenic to humans (Group 1) (in red)  
 Interventions with sufficient evidence of a cancer-preventive effect (in green)



<https://monographs.iarc.who.int/wp-content/uploads/2019/12/OrganSitePoster.PlusHandbooks.pdf>

# Tools a Toxicologist Might Use

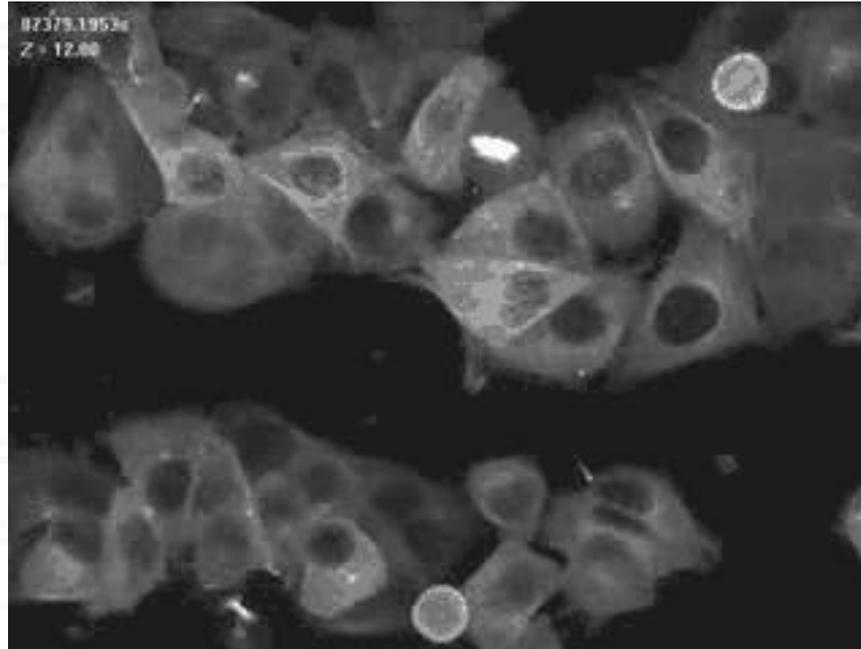
- Can conduct a **human health risk assessment**
  - Hazard identification
  - Dose-response assessment
  - Exposure assessment
  - Risk characterization
- Can conduct an **exposure reconstruction**
  - Utilize details of individual's risk factors to estimate a total dose of a chemical or substance to which they might have been exposed
  - Compare this dose to scientific studies of exposure in the literature



Was the individual exposed to a substance known to cause the disease they developed?

Was the dose received during exposure sufficient to have resulted in the disease?

Are there confounding exposures or conditions which may explain the disease?



**| Questions / Comments?**

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