Re-envisioning Carcinogenicity Assessment @ NTP

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“To improve public health through the development of data and knowledge that is translatable, predictive and timely.”
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Human Relevant & Impactful
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### Types of Breast Cancer

- **Ductal Carcinoma In Situ (DCIS)**
- **Invasive Ductal Carcinoma (IDC)**
- **IDC Type: Tubular Carcinoma of the Breast**
- **IDC Type: Medullary Carcinoma of the Breast**
- **IDC Type: Mucinous Carcinoma of the Breast**
- **IDC Type: Papillary Carcinoma of the Breast**
- **IDC Type: Cribriform Carcinoma of the Breast**
- **Invasive Lobular Carcinoma (ILC)**
- **Inflammatory Breast Cancer**
- **Lobular Carcinoma In Situ (LCIS)**
- **Male Breast Cancer**
- **Molecular Subtypes of Breast Cancer**
- **Paget's Disease of the Nipple**
- **Phyllodes Tumors of the Breast**
- **Metastatic Breast Cancer**
How many cancers are caused by exposure to carcinogens in the environment?

~4-20%

But the precise causes of most cancers are not known.

Value Proposition

What Are the Costs of Cancer?

The Agency for Healthcare Research and Quality estimates that the direct medical costs (total of all health care expenditures) for cancer in the US in 2015 were $80.2 billion.

According to a recent study by American Cancer Society epidemiologists, at least 42% of newly diagnosed cancers in the US – about 729,000 cases in 2018 – are potentially avoidable.

Source: Evercore ISI

I’m always amazed by the disconnect between what we see in the news and the reality of the world around us. As my late friend Hans Rosling would say, we must fight the fear instinct that distorts our perspective:
Causes of death in the US

Causes of deaths

- Heart Disease: 30.2%
- Cancer: 29.5%
- Road Incidents; Falls; Accidents: 10.7%
- Lower Respiratory Disease: 7.4%
- Alzheimer's disease: 5.6%
- Stroke: 4.9%
- Diabetes: 3.8%
- Drug overdose: 2.8%
- Kidney Disease: 2.7%
- Pneumonia & Influenza: 2.5%
- Suicide: 1.8%
- Homicide: 0.3%
- Terrorism: 0.1%

Google searches

- Heart Disease: 2.6%
- Cancer: 37%
- Road Incidents; Falls; Accidents: 10.7%
- Lower Respiratory Disease: 2.1%
- Alzheimer's disease: 2.0%
- Stroke: 6.5%
- Diabetes: 8.9%
- Drug overdose: 1.3%
- Kidney Disease: 1.1%
- Pneumonia & Influenza: 5.2%
- Suicide: 12.4%
- Homicide: 3.2%
- Terrorism: 7.2%

Media coverage:

- New York Times 2016:
  - Cancer: 13.5%
  - Alzheimer's disease: 1.9%
  - Lower Respiratory Disease: 2.6%
  - Stroke: 5%
  - Diabetes: 2.4%
  - Pneumonia & Influenza: 5.2%
  - Suicide: 10.6%

- The Guardian 2016:
  - Cancer: 12.7%
  - Alzheimer's disease: 1.4%
  - Lower Respiratory Disease: 2.6%
  - Stroke: 5%
  - Diabetes: 2.3%
  - Pneumonia & Influenza: 2.3%
  - Suicide: 14%

*This represents each cause's share of the top ten causes of death in the US plus homicides, drug overdoses and terrorism. Collectively these 13 causes accounted for approximately 88% of deaths in the US in 2016. Full breakdown of causes of death can be found at the CDC’s WONDER public health database: https://wonder.cdc.gov/

Based on data from Shen et al (2018) – Death: reality vs. reported. All data available at: https://owenshen24.github.io/charts-death

All data refers to 2016.
“Does [ Agent ] cause cancer?”

2 year Bioassay

Rodent Carcinogen: Yes, No, Maybe

Human Carcinogen: ?

“Cancer” (Hazard ID)
“Does [ Agent ] cause cancer?”

2 year Bioassay

Rodent Carcinogen: Yes, No, Maybe

Human Carcinogen: ?

“Cancer” (Hazard ID)

Agent X

How do we make this more translatable, predictive and timely?
Start incorporating human data
Identify those cancers likely associated with environmental exposures
“[Quantitative contribution] of Agent X to [cancer type Y] in [population Z]”

Develop a deep knowledge of specific cancer pathways
ER Pathway to Breast Cancer

From Morgan et al., 2016, Pharmacology & Therapeutics 165: 79-92
ER Pathway to Breast Cancer

“Tipping Point”
High likelihood of progressing to cancer

From Morgan et al., 2016, Pharmacology & Therapeutics 165: 79-92
ER Pathway to Breast Cancer

From Morgan et al., 2016, Pharmacology & Therapeutics 165: 79-92
"Does [Agent] cause cancer?"

"[Quantitative contribution] of Agent X to [cancer type Y] in [population Z]"

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Or Not

Agent X
Hypothesis-driven Research
Hypothesis-driven Research

Data / Knowledge Mining

Knowledge Integration

Computational Toxicology

Bioactivity Screening

In vitro Studies

Chronic in vivo Studies

Short term in vivo Studies

Communicate
• **Centralized cancer registries** in the United States conduct population-based surveillance of cancer incidence and mortality.
• State health departments (funded by CDC’s [National Program of Cancer Registries](http://www.cancer.gov) and NCI’s [Surveillance Epidemiology and End Results Program](http://seer.cancer.gov), collect cancer incidence data.

### Cancer Incidence

- **Liver cancer**
- **Leukemia**
- **Kidney cancer**
NIH All of US

The *All of Us* Research Program is a historic effort to gather data from one million or more people living in the United States to accelerate research and improve health.

Million Veteran Program (MVP)

MVP is a national, voluntary research program funded entirely by the Department of Veterans Affairs Office of Research & Development. The goal of MVP is to partner with Veterans receiving their care in the VA Healthcare System to study how genes affect health.
Next Steps

• Work with internal and external stakeholders to establish a problem statement and define scope
• Survey available resources
• Identify initial areas of focus
• Develop a strategic plan to set goals and establish timelines
• Develop a communication plan
Thank you

Questions?