

# What Is Cancer?

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# General COI Statement

I have no relevant relationships to disclose.

# Today's Presentation

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- **What is cancer?**  
**deadly; expensive; biologically complex;**  
**often preventable**
- **Cancer prevention: lessons learned about phytochemicals; obesity**
- **Mechanistic considerations and future directions**

# What is Cancer?

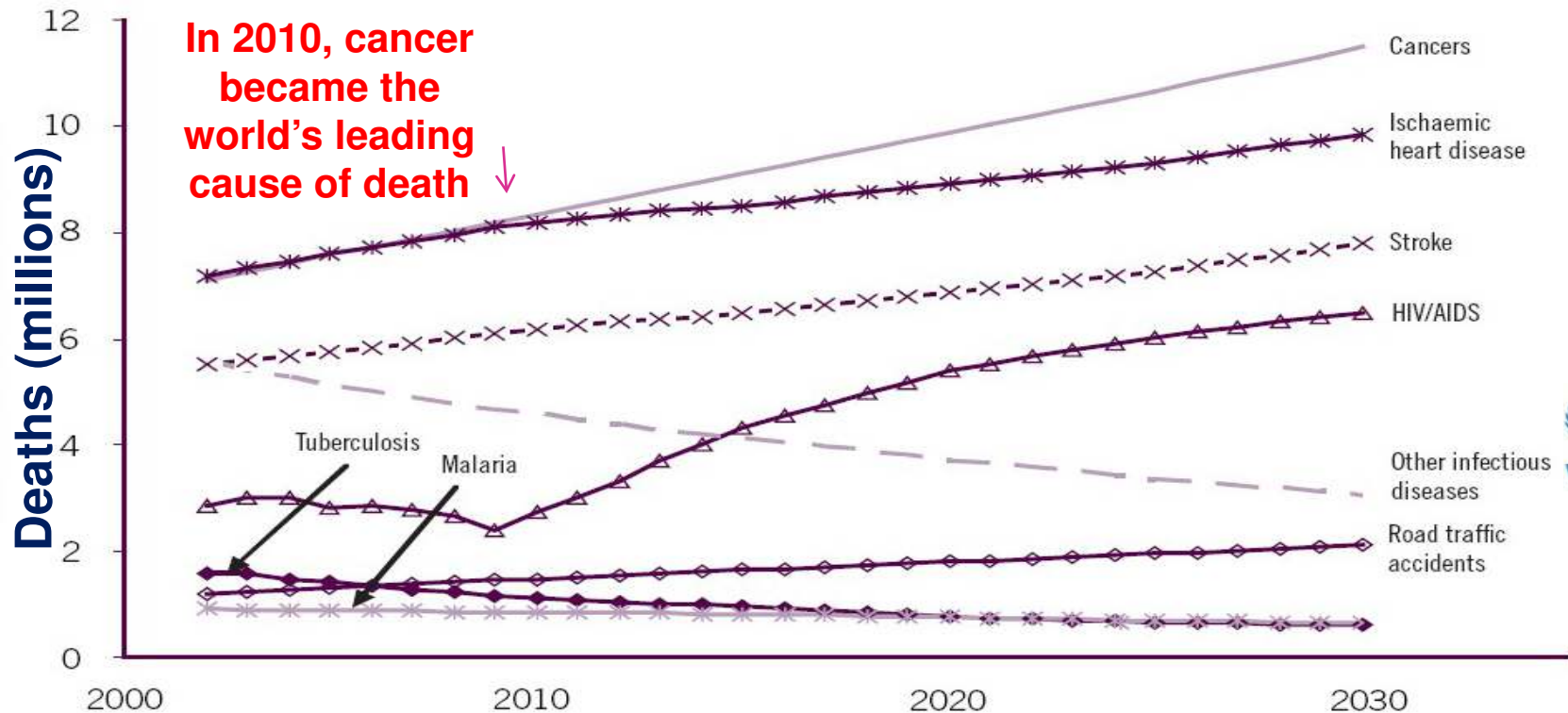
- ***Webster's:***

A malignant tumor of potentially unlimited growth that expands locally by invasion and systemically by metastasis.

- ***US National Cancer Institute:***

A **collection of related diseases** in which some of the body's cells begin to divide without stopping and spread to surrounding tissues. If the spread is not controlled, it can result in death.

# What is Cancer? A Major Killer



Global Cancer Report, IARC, 2016

# Leading Causes of Death, All Races and Both Genders, U.S.

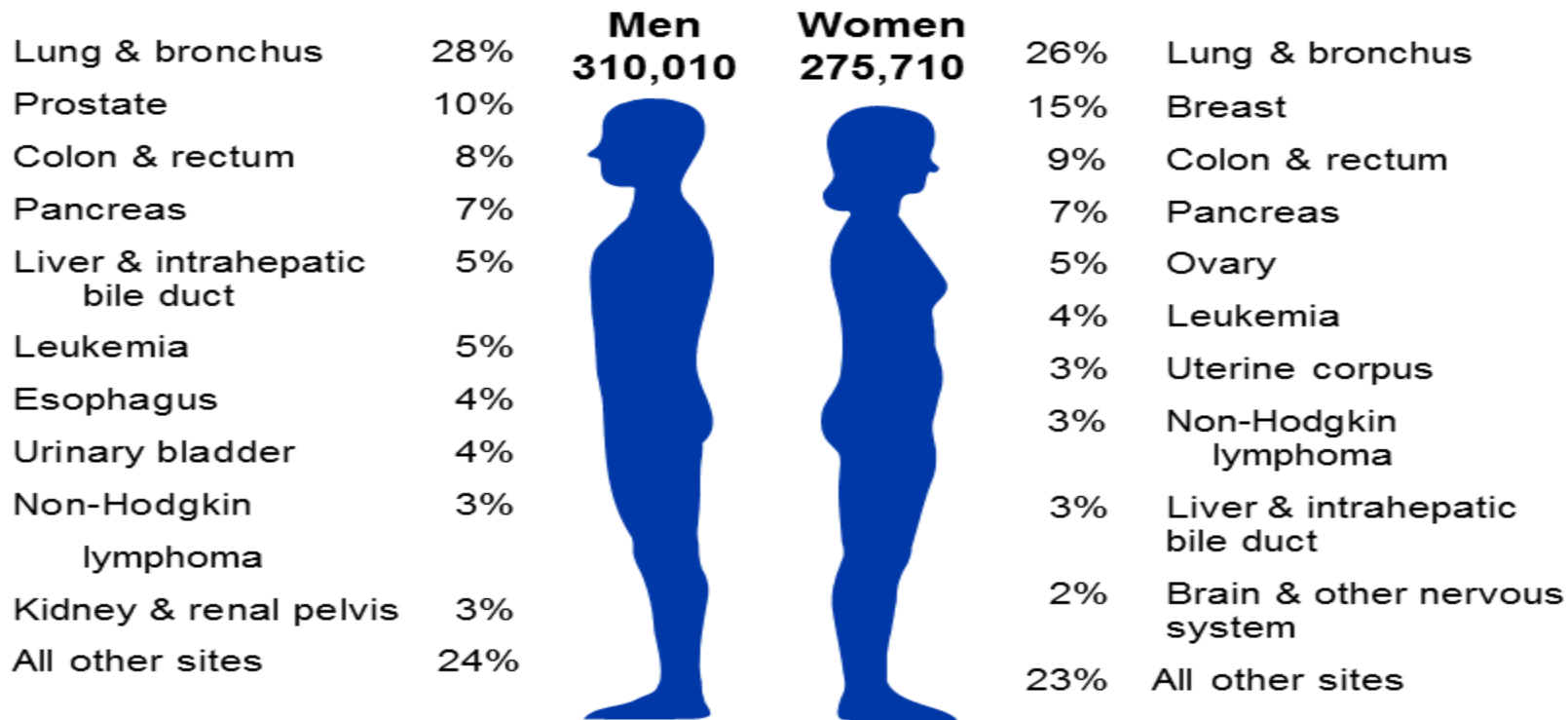
(NCHS, CDC, U.S. Department of Health and Human Services, 2016)

## Rank Order and Number of Deaths

<b>ALL CAUSES</b>	<b>2,467,819</b>
<b>Diseases of the heart</b>	<b>592,321 (24% of deaths)</b>
<b>Malignant neoplasms (cancer)</b>	<b>585,720 (24% of deaths)</b>
<b>Chronic lower respiratory disease</b>	<b>137,789</b>
<b>Cerebrovascular disease (stroke)</b>	<b>129,180</b>
<b>Unintentional injuries (accidents)</b>	<b>118,043</b>
<b>Alzheimer's disease</b>	<b>83,308</b>
<b>Diabetes mellitus</b>	<b>68,905</b>
<b>Nephritis, nephrotic syndrome, and nephrosis</b>	<b>50,472</b>
<b>Pneumonia and influenza</b>	<b>50,003</b>
<b>Suicide</b>	<b>37,793</b>

- **Lifetime risk of dying from cancer: 1 in 4**

## Estimated Cancer Deaths in the US in 2014



Source: American Cancer Society, 2016.

# What is Cancer? A Huge Economic Burden

## In the US in 2010:

**Cancer Treatment Costs: \$124.6 billion (~5% of health care \$)**  
**Projection by 2020: \$158-207 billion (depending on rate of ↑)**

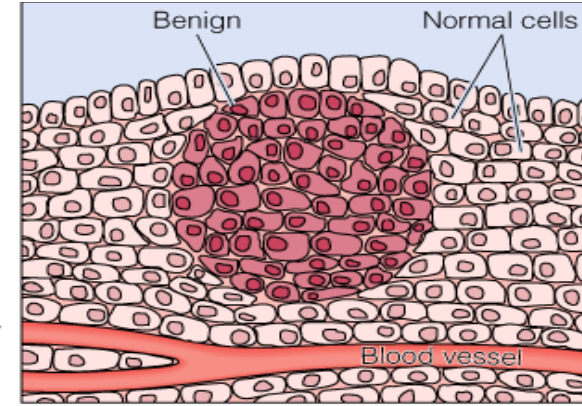
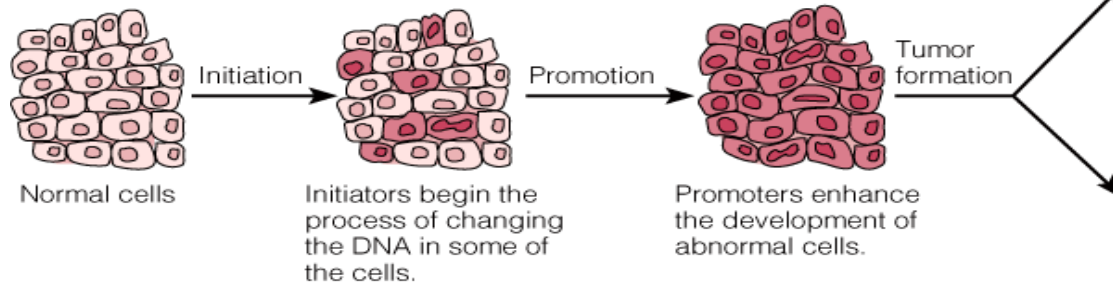
## Worldwide in 2008:

**Cancer Treatment Costs: ~\$850 billion**  
**Morbidity and Premature Mortality Costs: \$1.7 trillion**  
**(heart disease second at \$753 billion)**

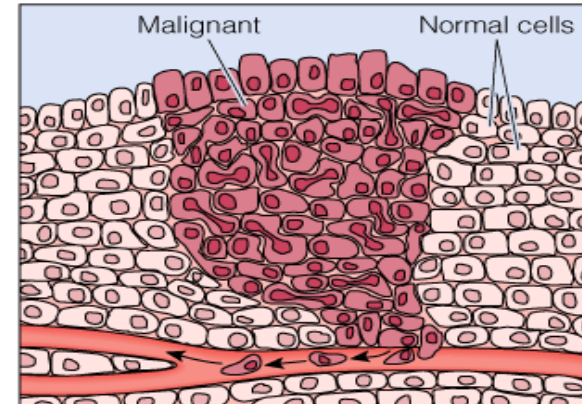


# What is Cancer?

## The final stage of a complex biological process



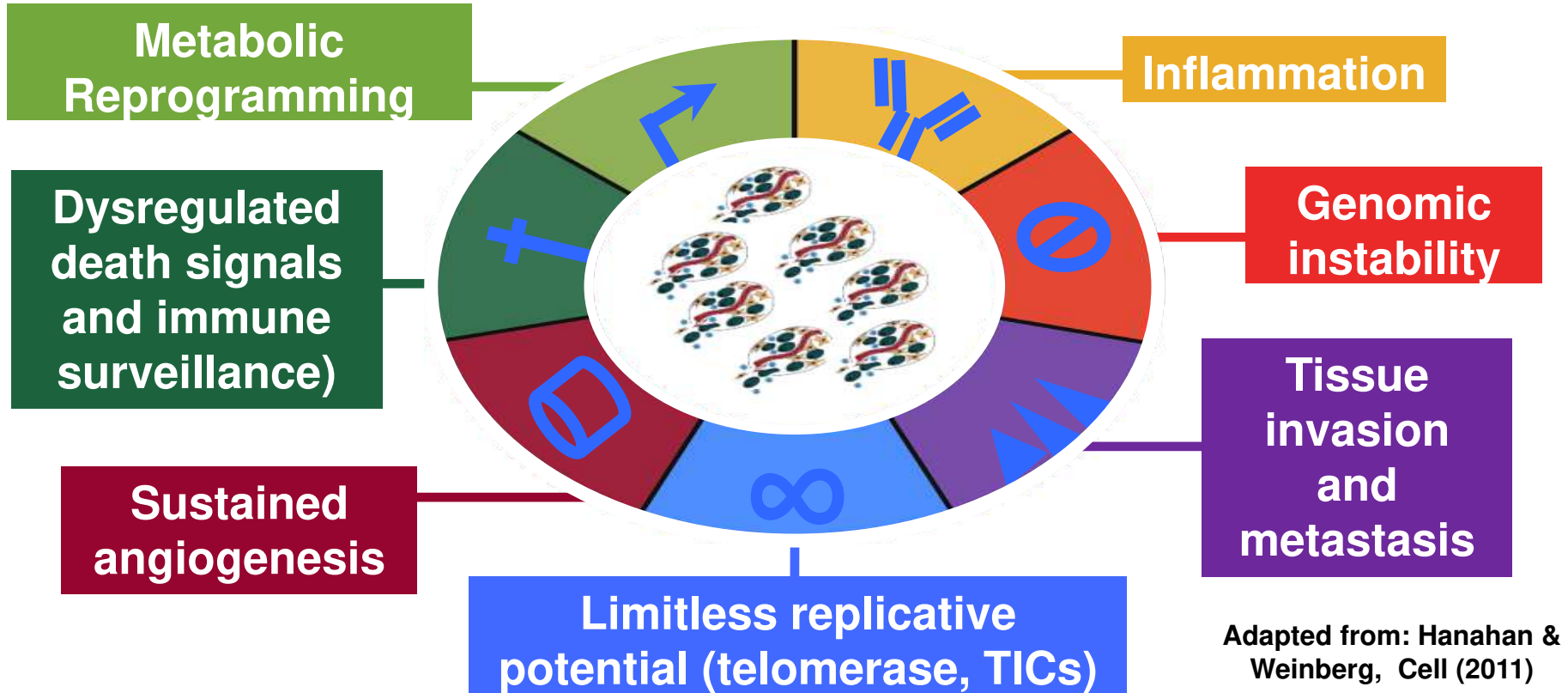
Noncancerous (benign) tumor



Cancerous (malignant) tumor releases cells into the bloodstream (metastasis)

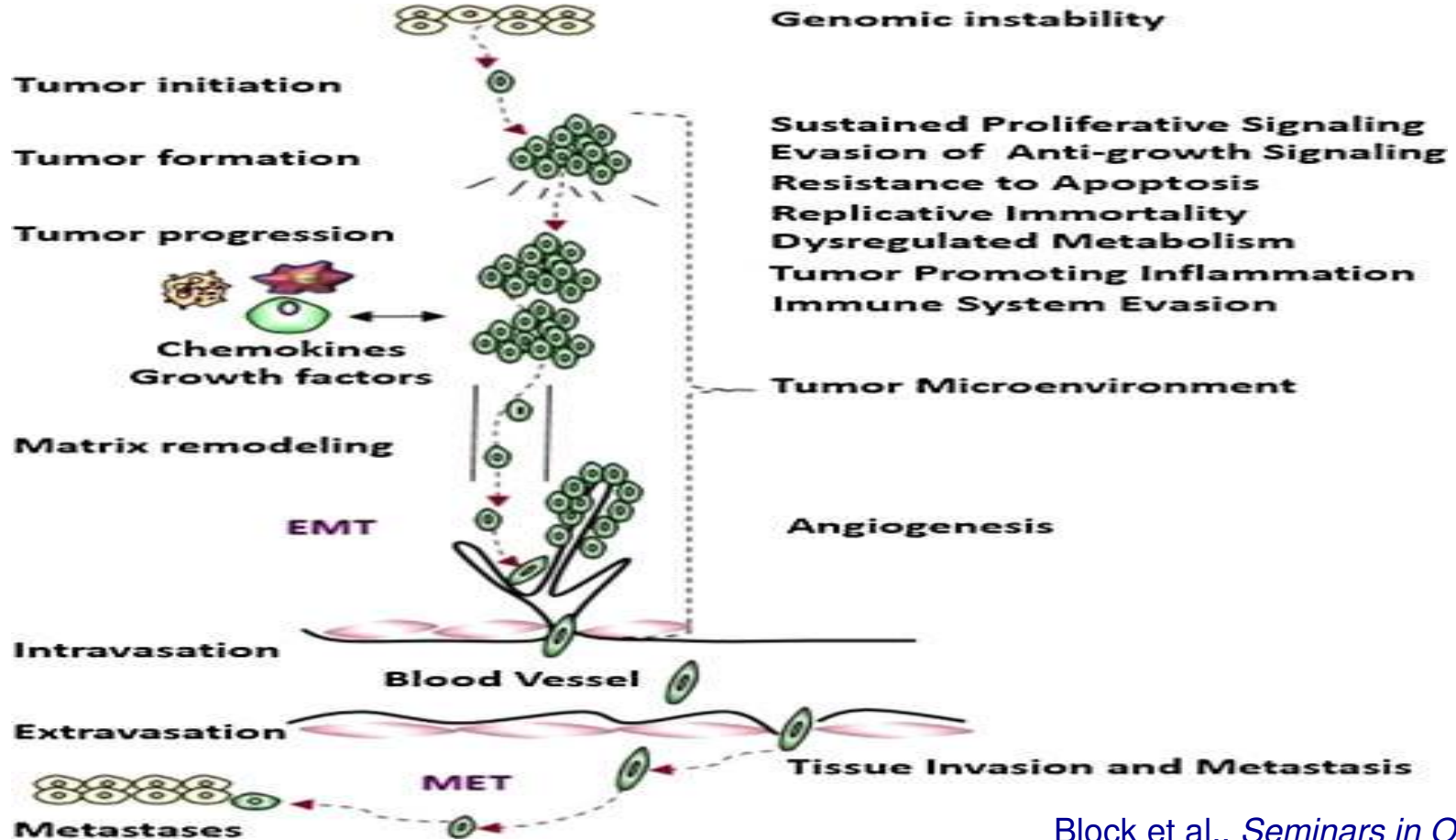
# Cancer: A Complex Foe

## *Hallmarks of all cancer cells*



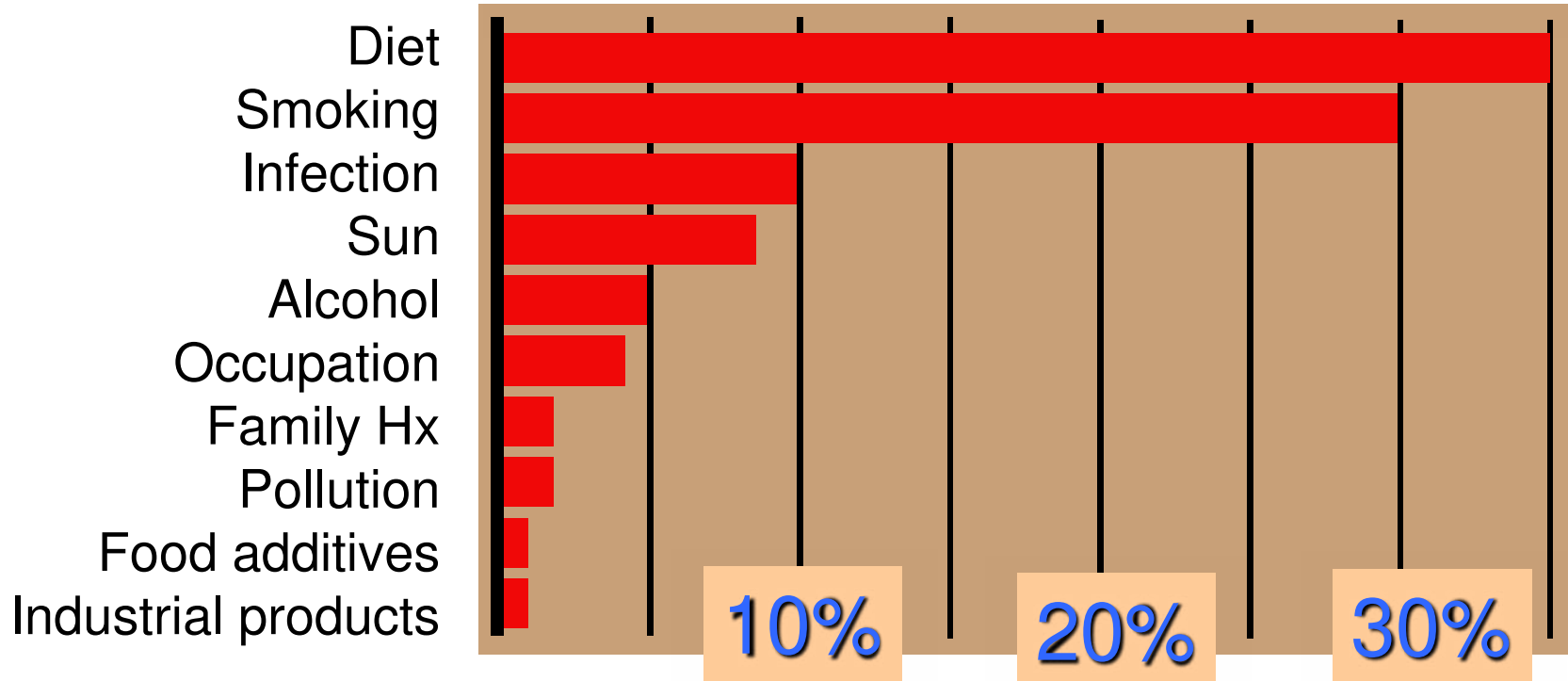
# Cancer Process

# Cancer Hallmarks



# What is Cancer? Preventable!

## Percent of Cancers Due to Each Factor



# 5-Year Survival Rates for Major Cancers in US

<u>Organ</u>	<u>If Localized</u>	<u>If Metastasized</u>
Colon	90%	10%
Breast	98%	26%
Prostate	100%	32%
Lung	49%	3%
Liver	28%	5%
Pancreas	10%	1%

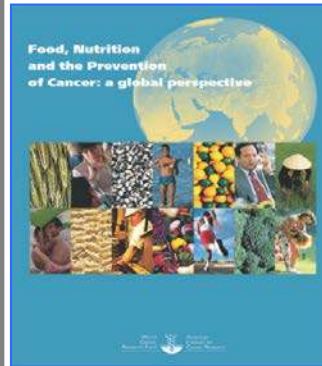
American Cancer Society, 2015

# Food, Nutrition, Physical Activity and the Prevention of Cancer: The AICR/WCRF Expert Reports

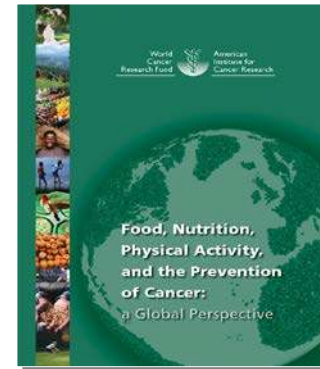


## AICR/WCRF Expert Report Recommendations

RECOMMENDATIONS
<b>BODY FATNESS</b> Be as lean as possible within the normal range of body weight
<b>PHYSICAL ACTIVITY</b> Be physically active as part of everyday life
<b>FOODS AND DRINKS THAT PROMOTE WEIGHT GAIN</b> Limit consumption of energy-dense foods Avoid sugary drinks
<b>PLANT FOODS</b> Eat mostly foods of plant origin
<b>ANIMAL FOODS</b> Limit intake of red meat and avoid processed meat
<b>ALCOHOLIC DRINKS</b> Limit alcoholic drinks
<b>PRESERVATION, PROCESSING, PREPARATION</b> Limit consumption of salt Avoid mouldy cereals (grains) or pulses (legumes)
<b>DIETARY SUPPLEMENTS</b> Aim to meet nutritional needs through diet alone
<b>BREASTFEEDING</b> Mothers to breastfeed; children to be breastfed
<b>CANCER SURVIVORS</b> Follow the recommendations for cancer prevention



1997



2007



2007-

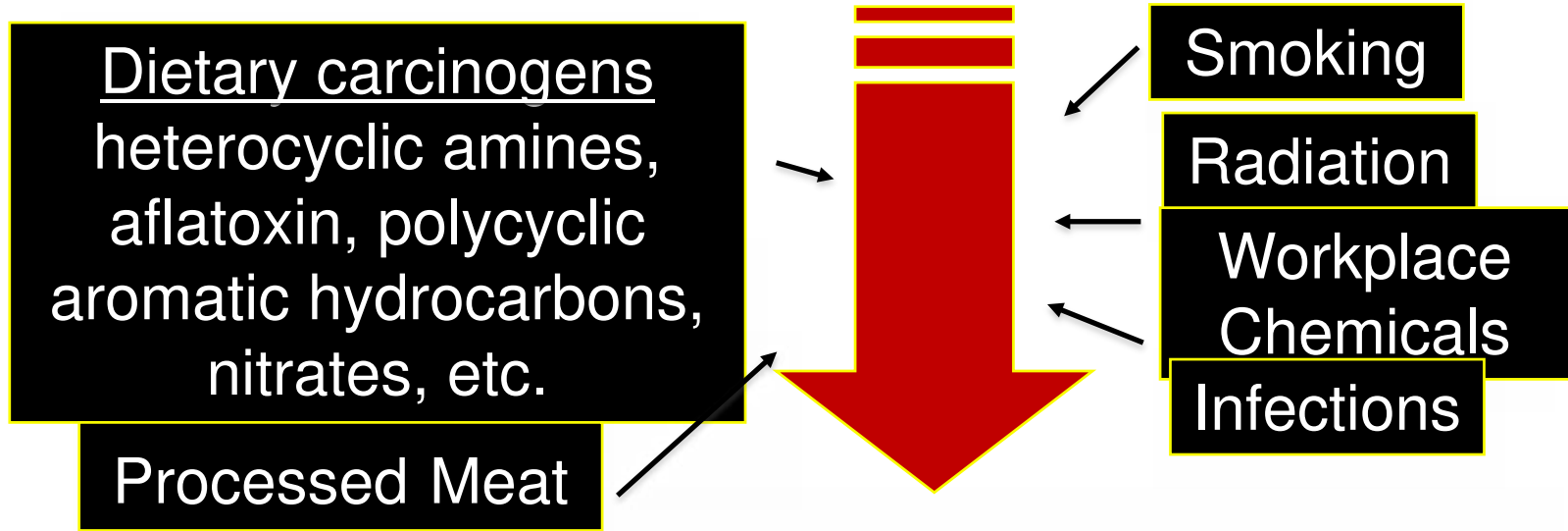
[www.aicr.org](http://www.aicr.org)





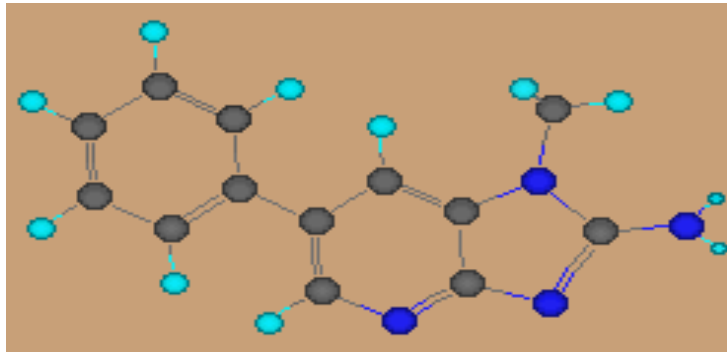


# Reduce Exposure to Pro-Cancer Agents

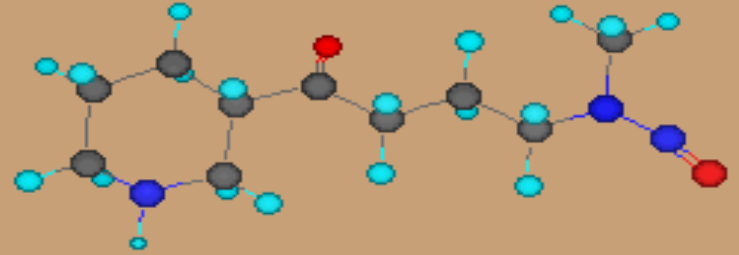


# Carcinogenesis

# Carcinogens in Foods



polycyclic aromatic  
hydrocarbons  
(charbroiled fat)



heterocyclic amines  
(meat cooked at high temp)



Folate

Polyphenolics

Stanols & sterols

Indole-3-carbinol

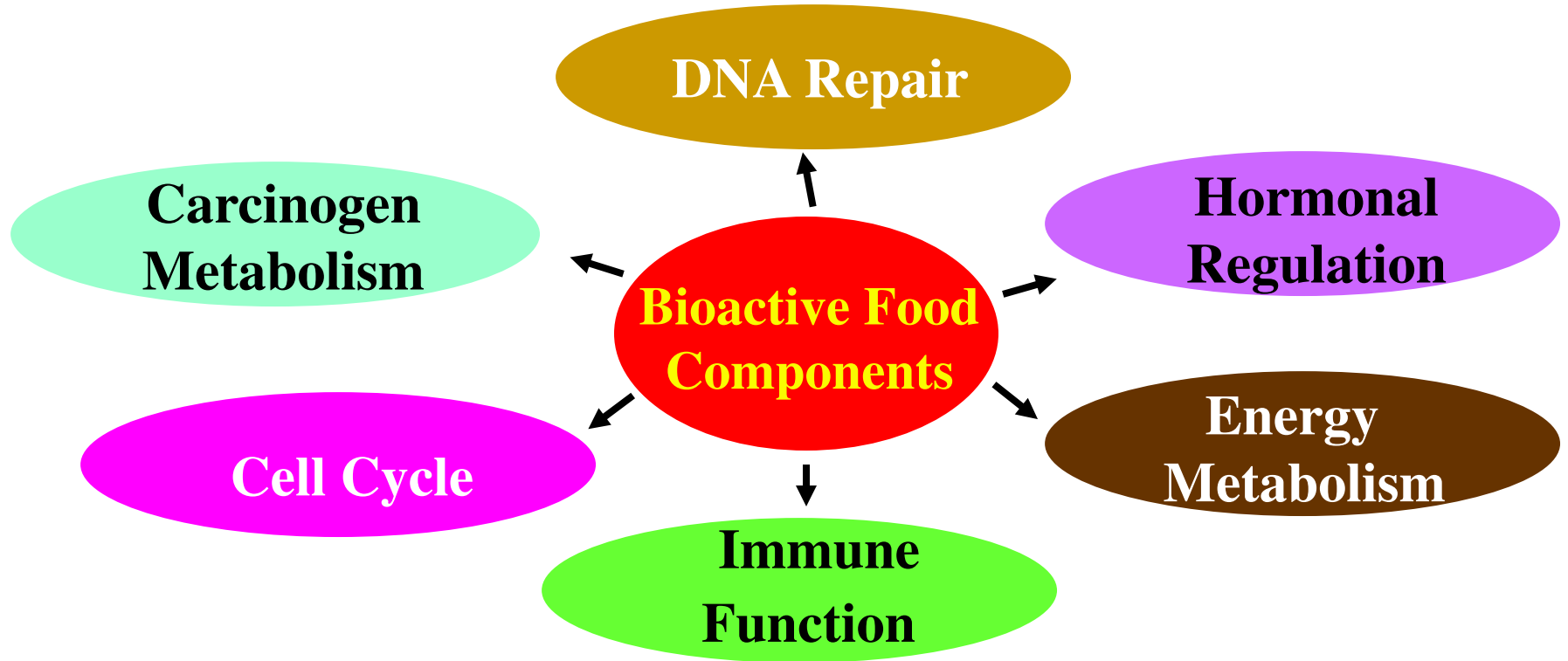
Flavonoids

Carotenoids

Anthocyanidins

**Fruits and Vegetables Contain Many Bioactive Components that Impact Carcinogenesis-Related Processes**

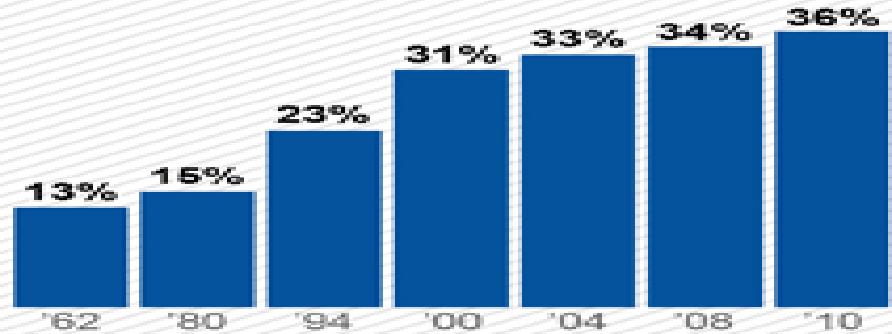
# Bioactive Food Components Influence Cancer Processes



# The US Obesity Epidemic

## Obesity over time

Percentage of obese adults, ages 20 to 74:



Source: Centers for Disease Control and Prevention

By Frank Poppa, USA TODAY

## Flegal, et al., JAMA 2016:

- 38% US Adults Obese (BMI >30.0 kg/m<sup>2</sup>)
  - 35.2% men, 40.5% women
- 7.7% US Adults Extremely Obese (BMI >40.0 kg/m<sup>2</sup>)
  - 5.5% men; 9.7% women

# Metabolic Syndrome

**Describes a state of metabolic dysregulation characterized by:**

- Insulin resistance, hyperglycemia\*
- Dyslipidemia (↑triglycerides\*, ↓HDL-C\*)
- ↑Waist circumference\*
- Hypertension\*
- Proinflammatory state (↑cytokines, ↑chemokines)
- Vascular perturbations (↑PAI-1, ↑VEGF)
- Altered adipokines (↑leptin, ↓adiponectin)
- Elevated insulin-like growth factor (IGF)-1

- **Associated with many types of cancer**

25% (144K) cancer deaths/year in US caused by overweight/obesity

(Calle, et al., *NEJM* 2003; Colditz, et al. *Science Transl Med*, 2012)



## American Society of Clinical Oncology Position Statement on Obesity and Cancer

*Jennifer A. Ligibel, Catherine M. Alfano, Kerry S. Courneya, Wendy Demark-Wahnefried, Robert A. Burger, Rowan T. Chlebowski, Carol J. Fabian, Ayca Gucalp, Dawn L. Hershman, Melissa M. Hudson, Lee W. Jones, Madhuri Kakarala, Kirsten K. Ness, Janette K. Merrill, Dana S. Wollins, and Clifford A. Hudis*

### Obesity:

- a central challenge in cancer prevention and care
- leading preventable cause of cancer in US
- can increase risk of cancer recurrence, lower survival
- by 2030, ~500,000 Americans/yr diagnosed with obesity-related cancer unless corrective action

SPECIAL REPORT

# Body Fatness and Cancer — Viewpoint of the IARC Working Group

Béatrice Lauby-Secretan, Ph.D., Chiara Scoccianti, Ph.D., Dana Loomis, Ph.D.,  
Yann Grosse, Ph.D., Franca Bianchini, Ph.D., and Kurt Straif, M.P.H., M.D., Ph.D.,  
for the International Agency for Research on Cancer Handbook Working Group

*NEJM*, August 25, 2016



# IARC Handbook of Cancer Prevention

## Volume 16: Body Fatness and Cancer

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- Identified 13 cancer types in which there is sufficient evidence that avoidance of excess body fatness prevents those cancers. colon and rectum, oesophagus (adenocarcinoma), kidney (renal cell), breast (post-menopausal), endometrium, gastric cardia,liver, gall bladder, pancreas, ovary, thyroid, multiple myeloma, meningioma.
- Intentional weight loss in obese people may reduce risk of some cancers (based primarily on bariatric surgery studies), but the number and quality of weight loss studies was deemed insufficient for formal evaluation.

# IARC Handbook of Cancer Prevention

## Volume 16: Body Fatness and Cancer

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- Obesity consistently promotes cancer in rodent models of the same cancer types shown to be associated with obesity in humans; number of studies for many sites is limited.
- Sufficient evidence in experimental models for a cancer preventive effect of calorie restriction (which prevents obesity) for many cancer sites.
- Limited preclinical evidence that intentional weight loss (if severe enough) can reverse the procancer effects of obesity.

# IARC Handbook of Cancer Prevention

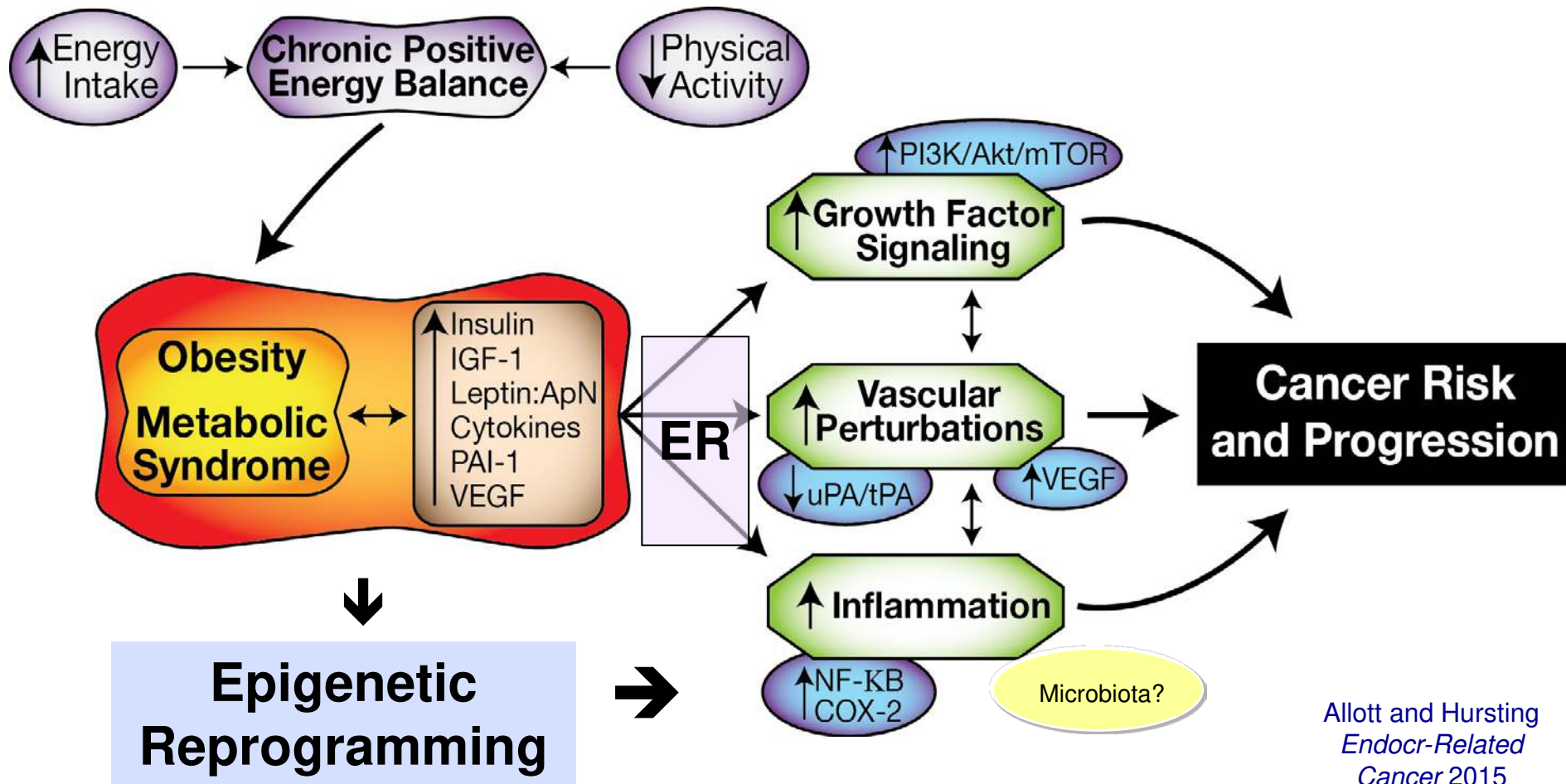
## Volume 16: Body Fatness and Cancer

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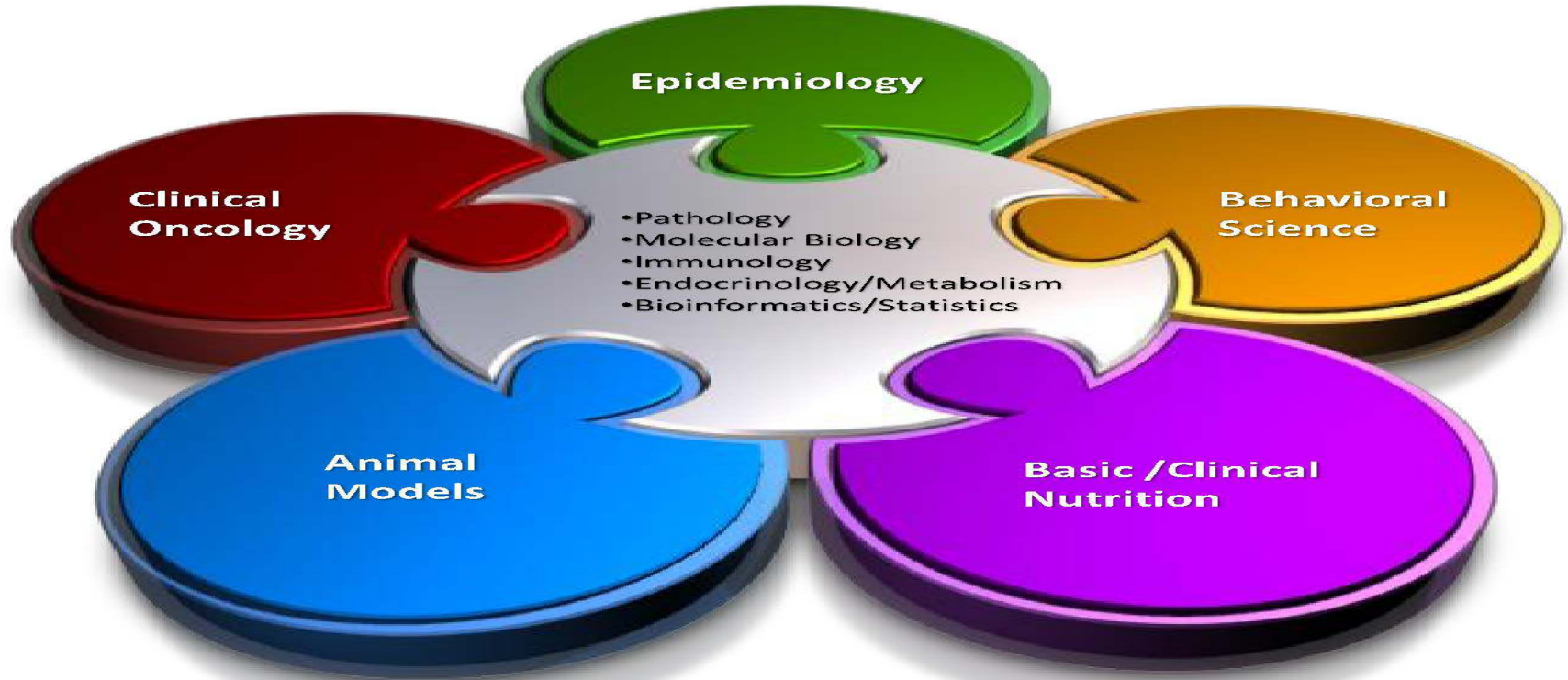
### Underlying Mechanisms

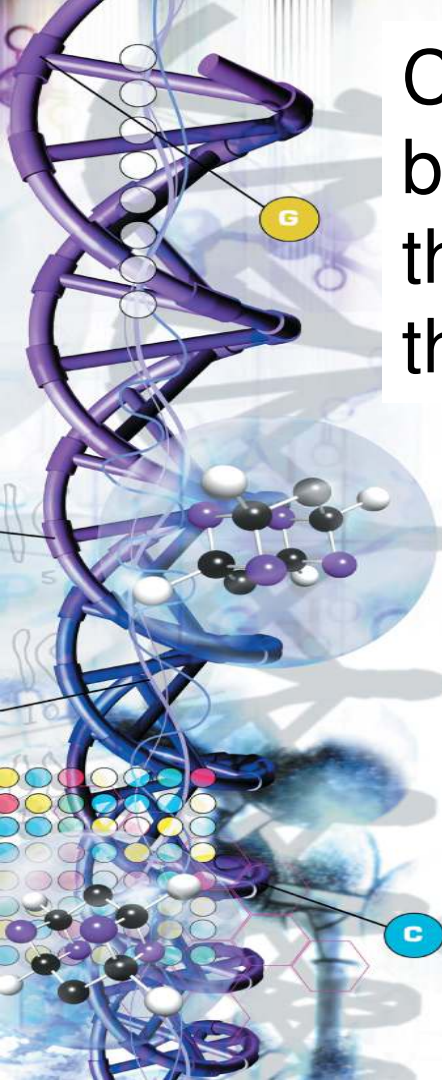
- Obesity is associated with significant metabolic and endocrine abnormalities, including alterations in sex-hormone metabolism, insulin/insulin-like growth factor (IGF) signaling, adipokines, and inflammatory pathways
- Possible contributors (but limited evidence): gut microbiome, angiogenesis, bioenergetic reprogramming, stemness, antitumor immune responses, and **epigenetic reprogramming**

# Obesity and Cancer: Underlying Mechanisms

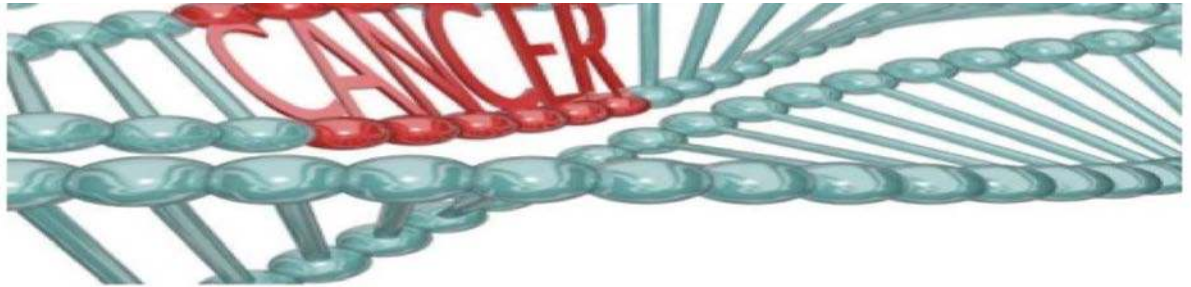


# Energy Balance and Cancer Prevention: Transdisciplinary Research Approaches





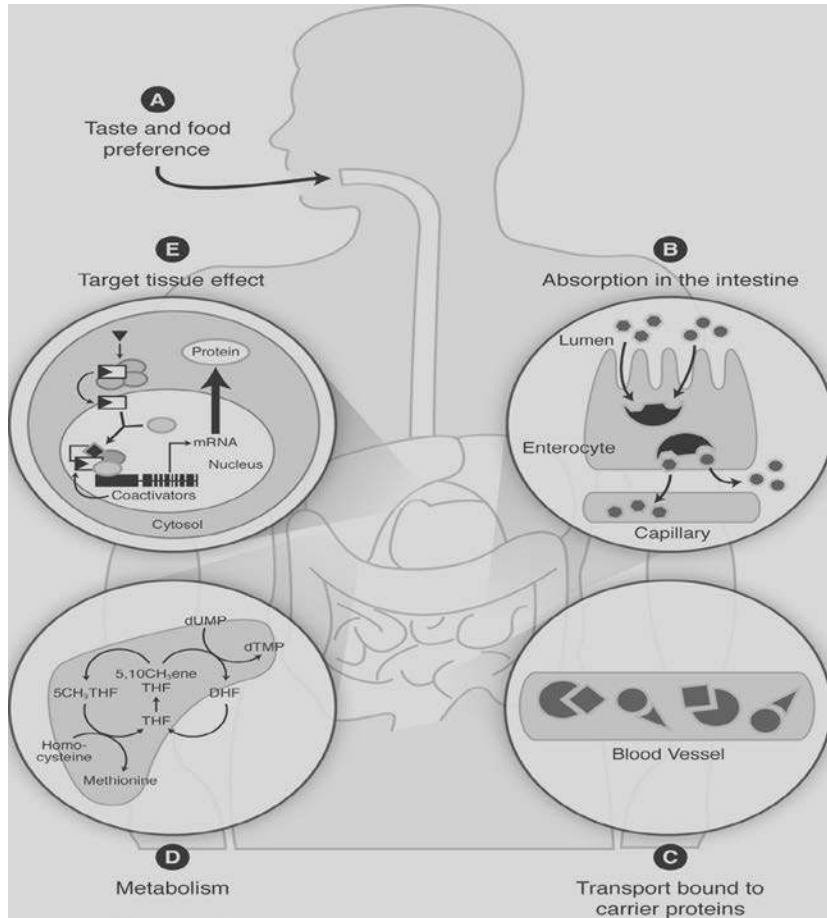
Cancer results from a complex interaction between an individual's genetic make-up and the environmental (including dietary) agents they are exposed to.



### Challenge in Preventing or Treating Cancer:

- **Every tumor is different**
- **Every person is different**

# Genotype Influences the Response to Diet



- Food preference
- Food tolerance
- Absorption
- Transport
- Metabolism
- Effects in target tissues

# Take Home Messages from Today's Presentation

- **What is cancer?** A group of diseases characterized by uncontrolled growth and spread of abnormal cells; major killer; expensive; complex but increasingly understood biology; many cancers preventable, with diet a key factor.
- **Diet and cancer prevention:** current focus on plant-based dietary patterns and obesity prevention/reversal
- **Future progress:** transdisciplinary research leading to effective mechanism-based approaches; personalized.