

Early Life Exposure and Disease Health Risk

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Outline of the presentation

Factors that contributes to increased cancer risk

Effect of early life exposures to environmental agents on health diseases:

prostate cancer

uterine cancer

metabolic diseases

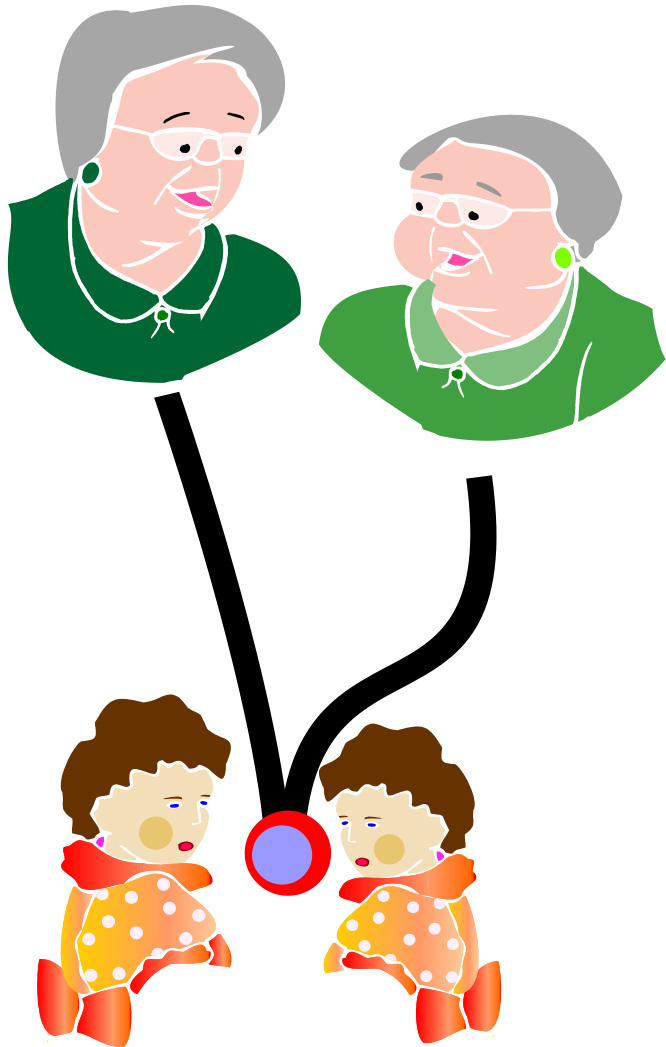
reproduction

Twin studies show that there must be factors separate from DNA that impact health and longevity

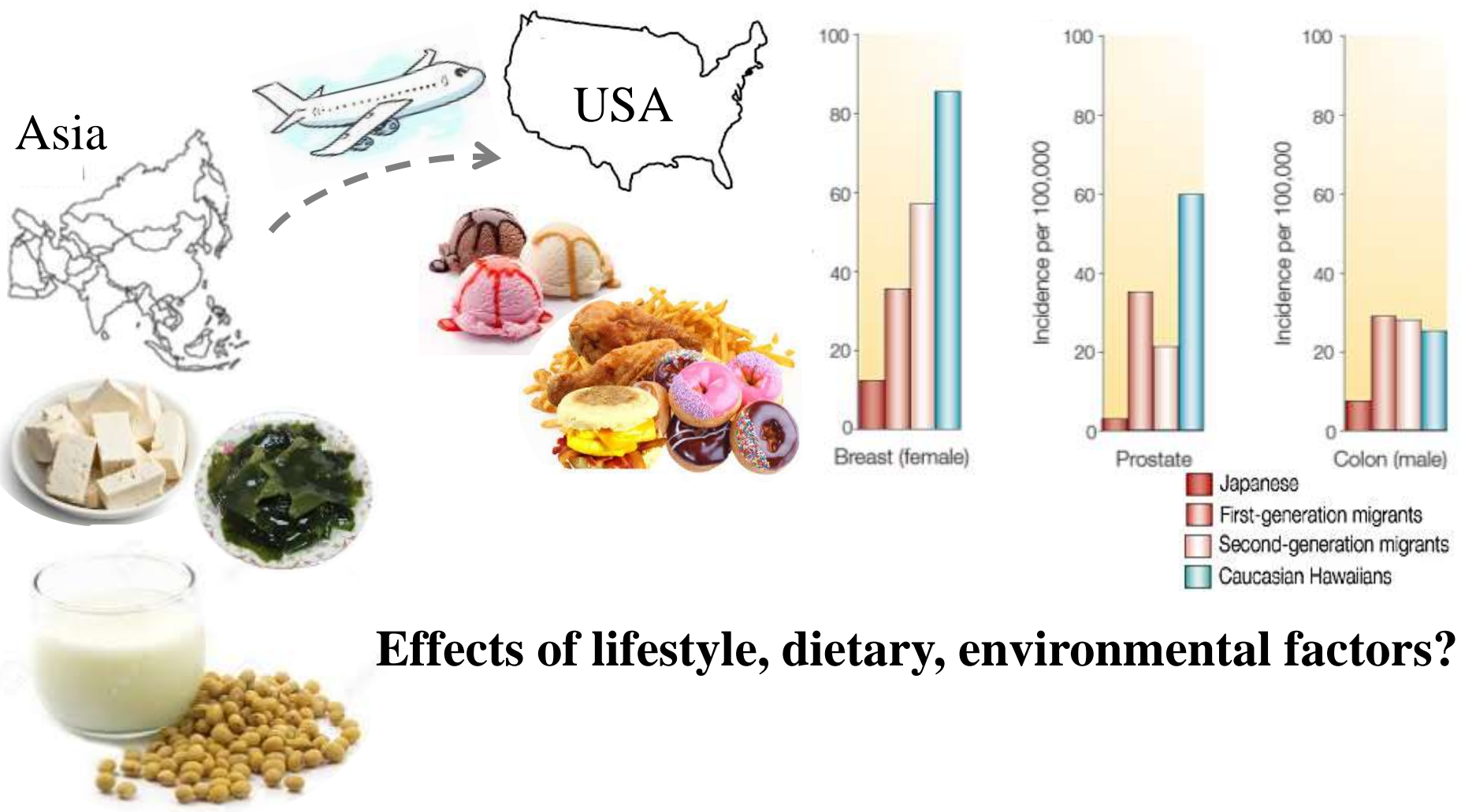
Environmental differences can make one twin more vulnerable to disease than the other (e.g., smoking and diet)

Genomic DNA is virtually identical

Their health outcome and behavior may change over time depending on the environment after birth



Cancer incidence is higher in immigrants: Incident rate increases in subsequent generations

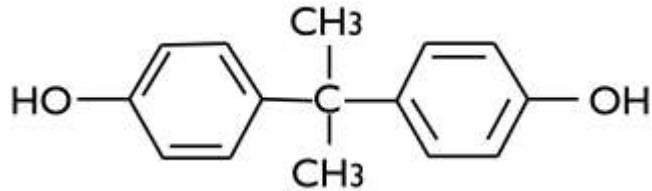


Effects of lifestyle, dietary, environmental factors?

Popkin and Udry, 1998; Singh and Hiatt, 2006; Ziegler et al, 1993

Bisphenol A (BPA)

- the endocrine disruptor



Production of **1.6 billion pounds** in North America

95% of adults surveyed have detectable concentrations of total urinary BPA
(*Calafat et al 2005*)

BPA is ubiquitously present in the environment

Polycarbonate plastics



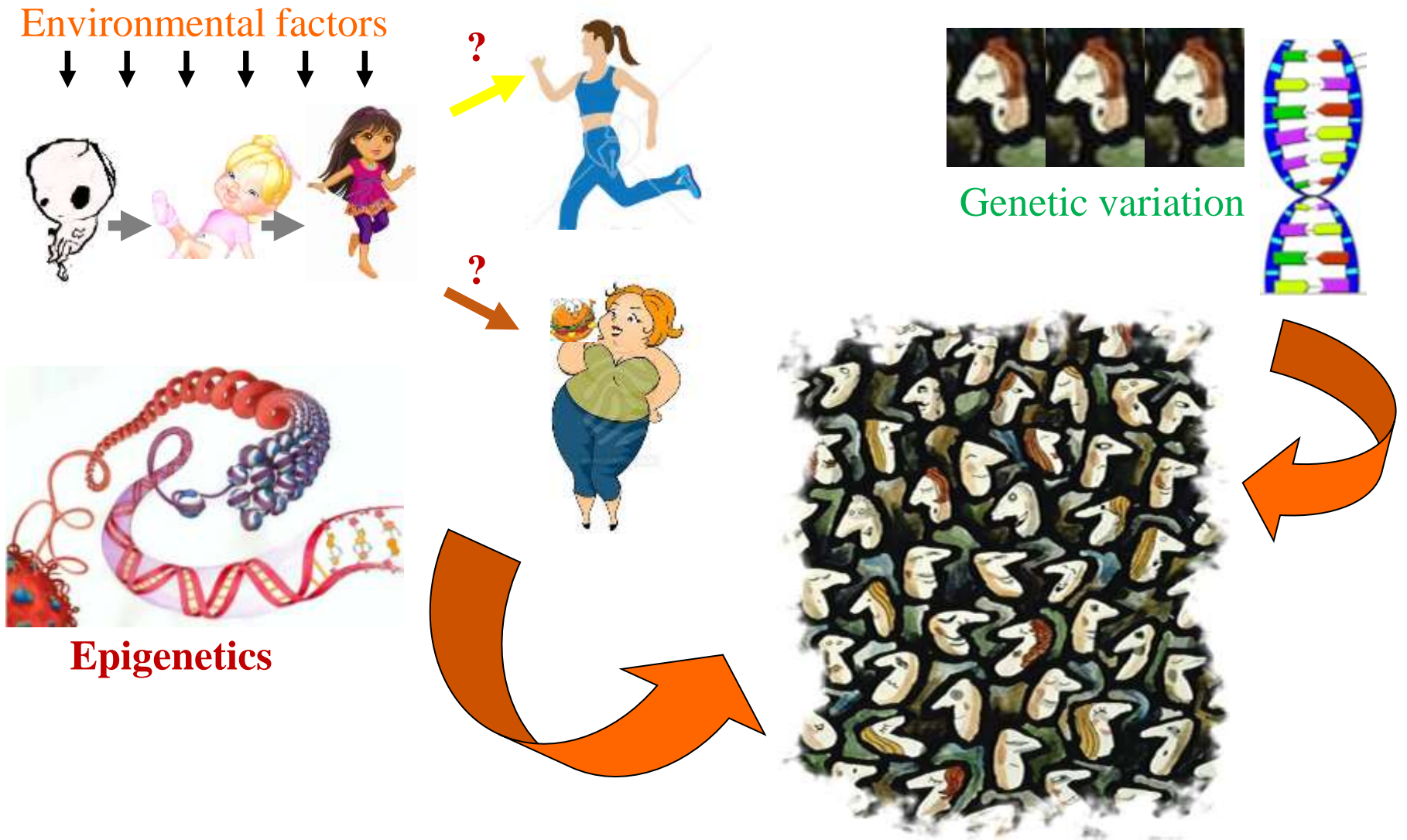
Epoxy resins



Paper bills and receipts



Epigenetics serves as an **interface** between the **environment** and the inherited **genome**



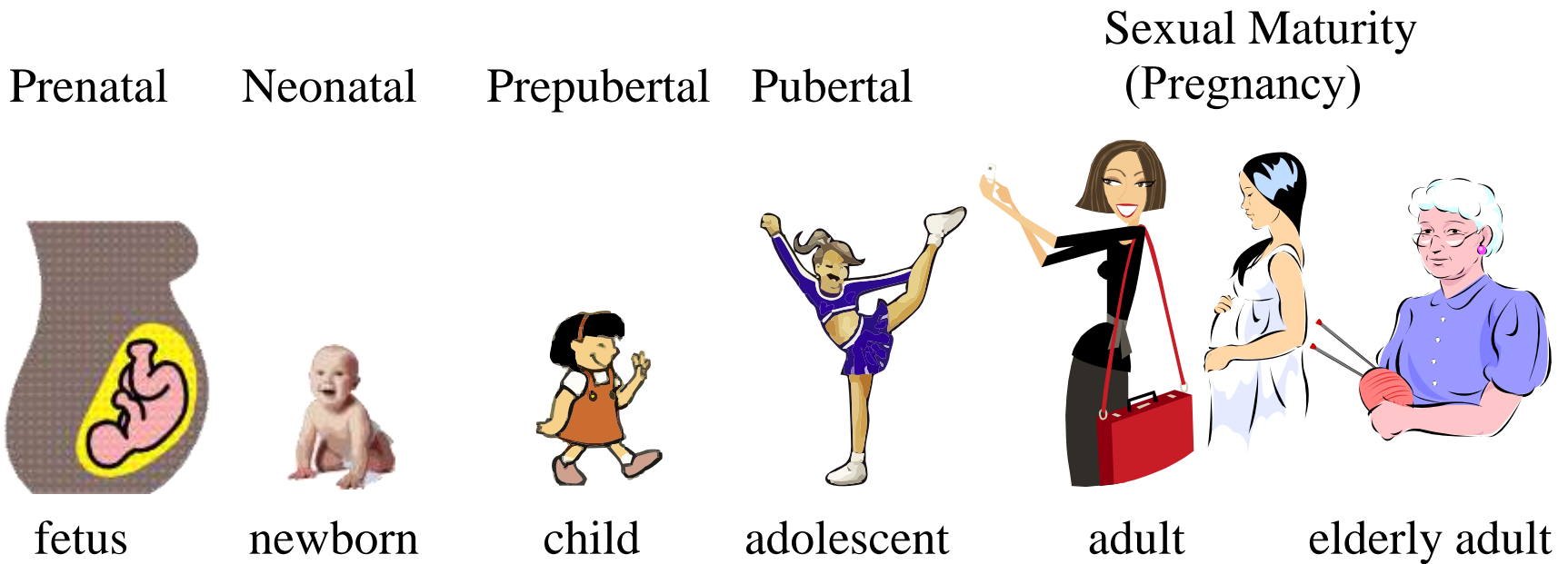
Early origins of human diseases

Epidemiologic studies now support an early origin of adult human diseases.

Example:

association between **low birth weight** and a greater risk of **coronary heart disease, hypertension, stroke, depression, type 2 diabetes, and osteoporosis** in later life

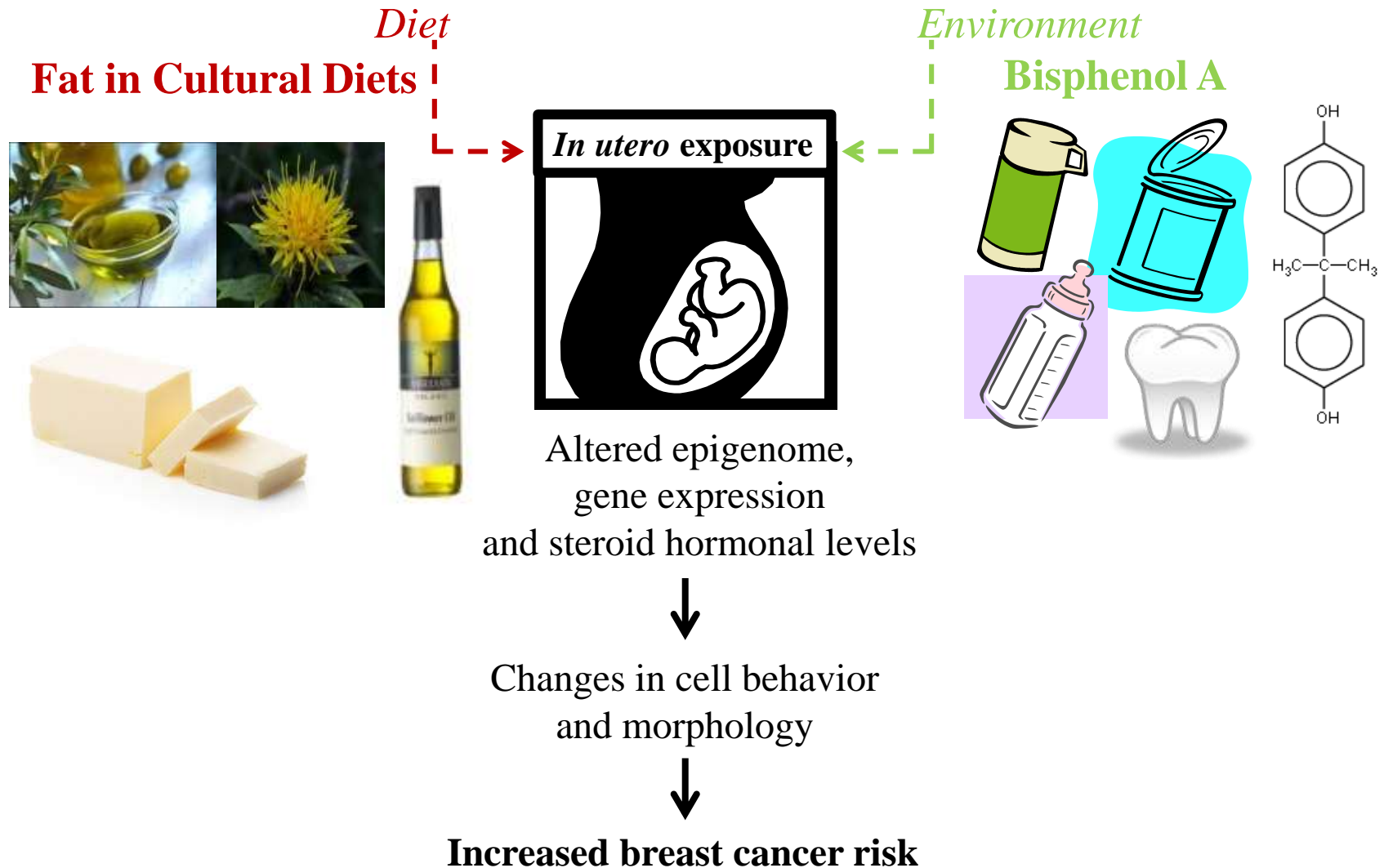
Developmental Plasticity: Windows of Susceptibility



Is breast cancer of fetal origin?

Hypothesis

In utero exposure to dietary fats and environmental agents increases breast cancer risk later in life



In utero exposure to estradiol and bisphenol A reprograms prostate cancer (PCa) risk

Before birth

Young

Old

Caucasians

Lower estradiol level



Lower PCa incidence

African-Americans

Higher estradiol level



Higher PCa incidence



Bisphenol A



??

PCa incidence

Henderson and Ross 1988

Neonatal estrogen reprogramming increases later life prostate cancer risk

Sprague Dawley rat

No estrogen (E)



Adult hormonal
Treatment on
PND 90-200

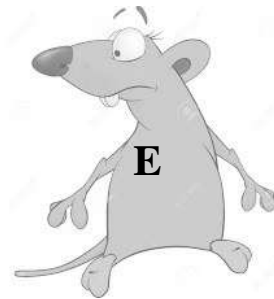


Low cancer
Incidence (30%)

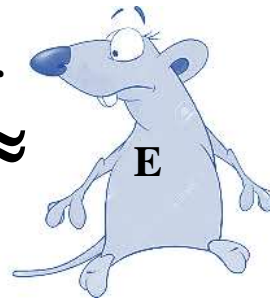
Neonatal estrogen treatment
on post-natal day (PND)1, 3, 5



Adult hormonal
Treatment on
PND 90-200



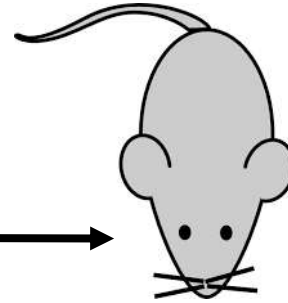
High cancer
Incidence \approx
(100%)



Noble rat

In utero exposure to diethylstilbestrol induces uterine cancer risk and infertility in later life

Diethylstilbestrol (DES)
- Synthetic estrogen



Increased risk of uterine adenocarcinoma

Reproductive Tract Abnormalities

normal cervix with a "hood"



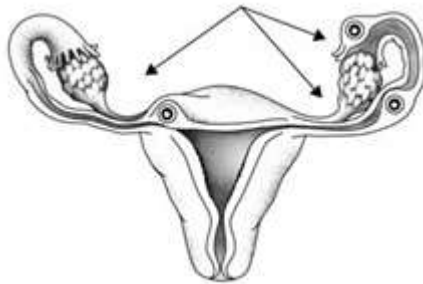
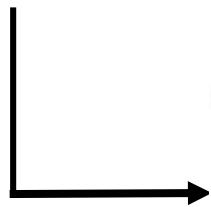
normal

a "T"

shaped uterus

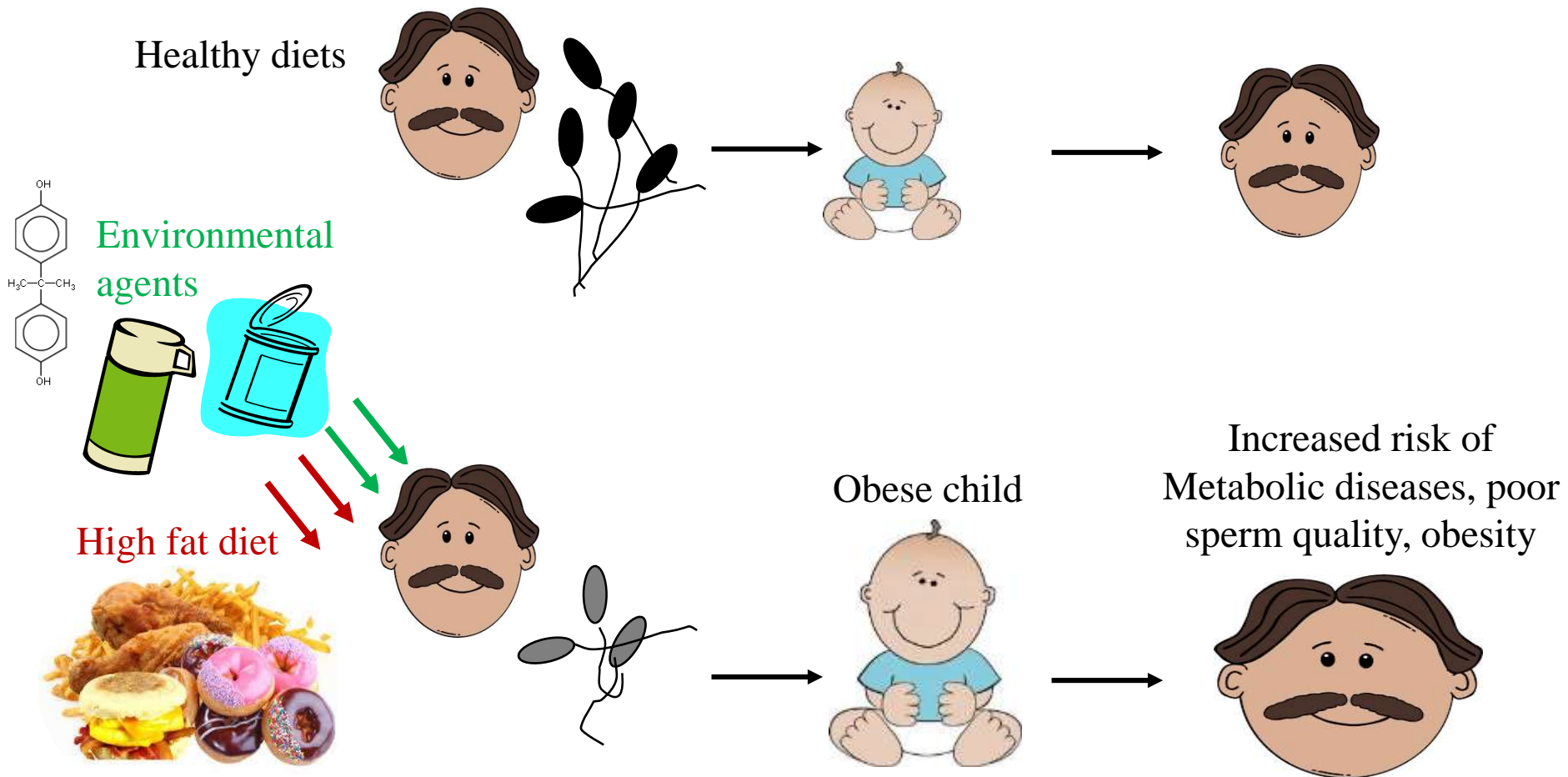


Higher miscarriage and infertility rates



Increased incidence of ectopic pregnancy

Paternal exposure to high fat diet and environmental agents increases health risk in offspring



Early life exposures to environmental agents and different lifestyle factors affects later-life cancer risk

The End

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