

University of Cincinnati Cancer Institute

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COMPREHENSIVE LUNG CANCER CENTER

# Food for Thought: Can Diet Play a Role in Lung Cancer?

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# Overview

- Epigenetics & Telomeres
- Anti-Inflammatory Diet
- Antioxidants
- Diet Guidelines & Resources

# Questions to Discuss

- Does what you eat really contribute to the development of cancer?
- What does research say about the impact of different types of foods on cancer and its treatment?

# What is Integrative Medicine?

*Integrative Medicine* is the practice of medicine that reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic approaches, healthcare professionals, and disciplines to achieve optimal health and healing.

- Consortium of Academic Health Centers for Integrative Medicine (2004)

# Epigenetics



# Epigenetics

- Literally “above” or “on top of” genetics
- Refers to external modifications to DNA that turn genes either “on” or “off”
- Do not change the DNA sequence, but instead, affect how cells “read” genes

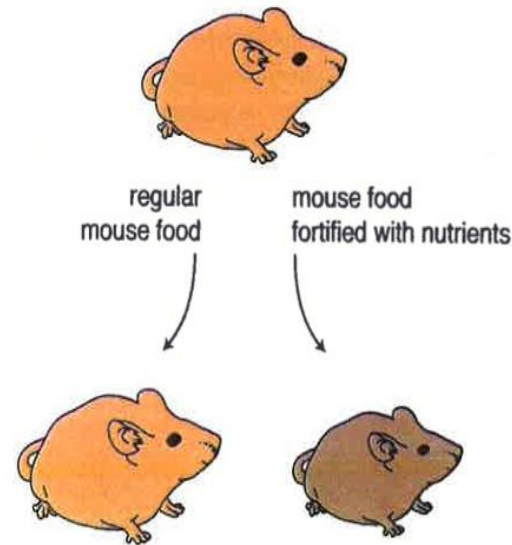
# Epigenetics in Action: The Agouti Mouse

Yellow agouti mice become obese and have a high risk of diabetes, cancer and shortened lifespan.

Brown agouti mice are thin, with a normal lifespan and reduced risk of diabetes and cancer.



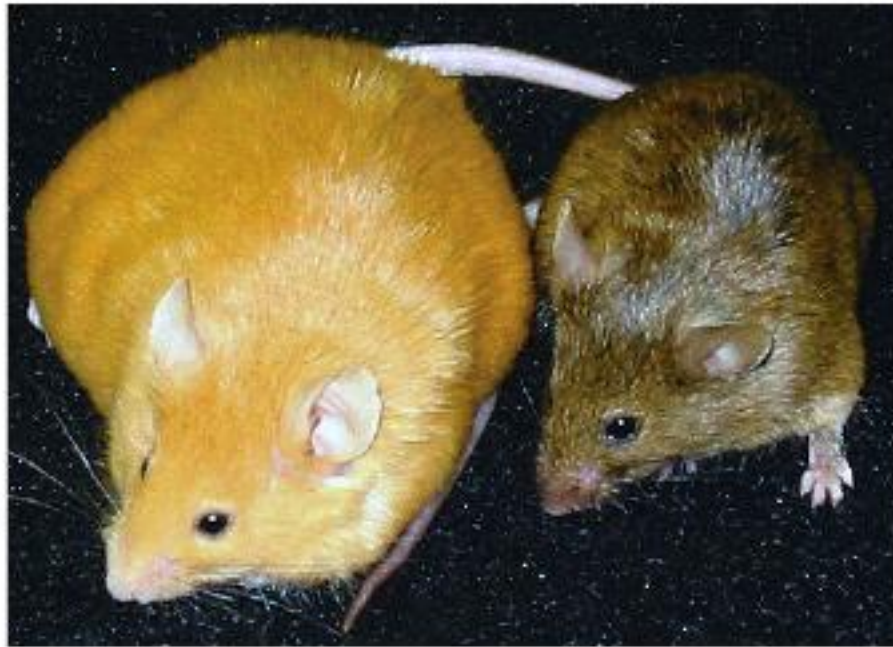
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# Epigenetics in Action

These Two Mice are Genetically Identical and the Same Age



While pregnant, both of their mothers were fed Bisphenol A (BPA) but **DIFFERENT DIETS**:

The mother of this mouse received a **normal mouse diet**

The mother of this mouse received a diet **supplemented** with choline, folic acid, betaine and vitamin B12



# Epigenetics



# How Do We Alter Gene Expression?

- Diet
- Exercise
- Stress Reduction



## Histone modifications



Tomatoes  
(Lycopene)



Turmeric  
(Curcumin)



Cinnamon  
(Coumaric acid)



Cashew nuts  
(Anacardic acid)



Apples  
(Phloretin)



Soybean  
(Genistein)



Tea  
(EGCG)



Grapes  
(Resveratrol)



Citrus  
(Hesperidin)



Coffee  
(Caffeic acid)



Broccoli  
(Isothiocyanates)



Garlic  
(Allyl mercaptan)

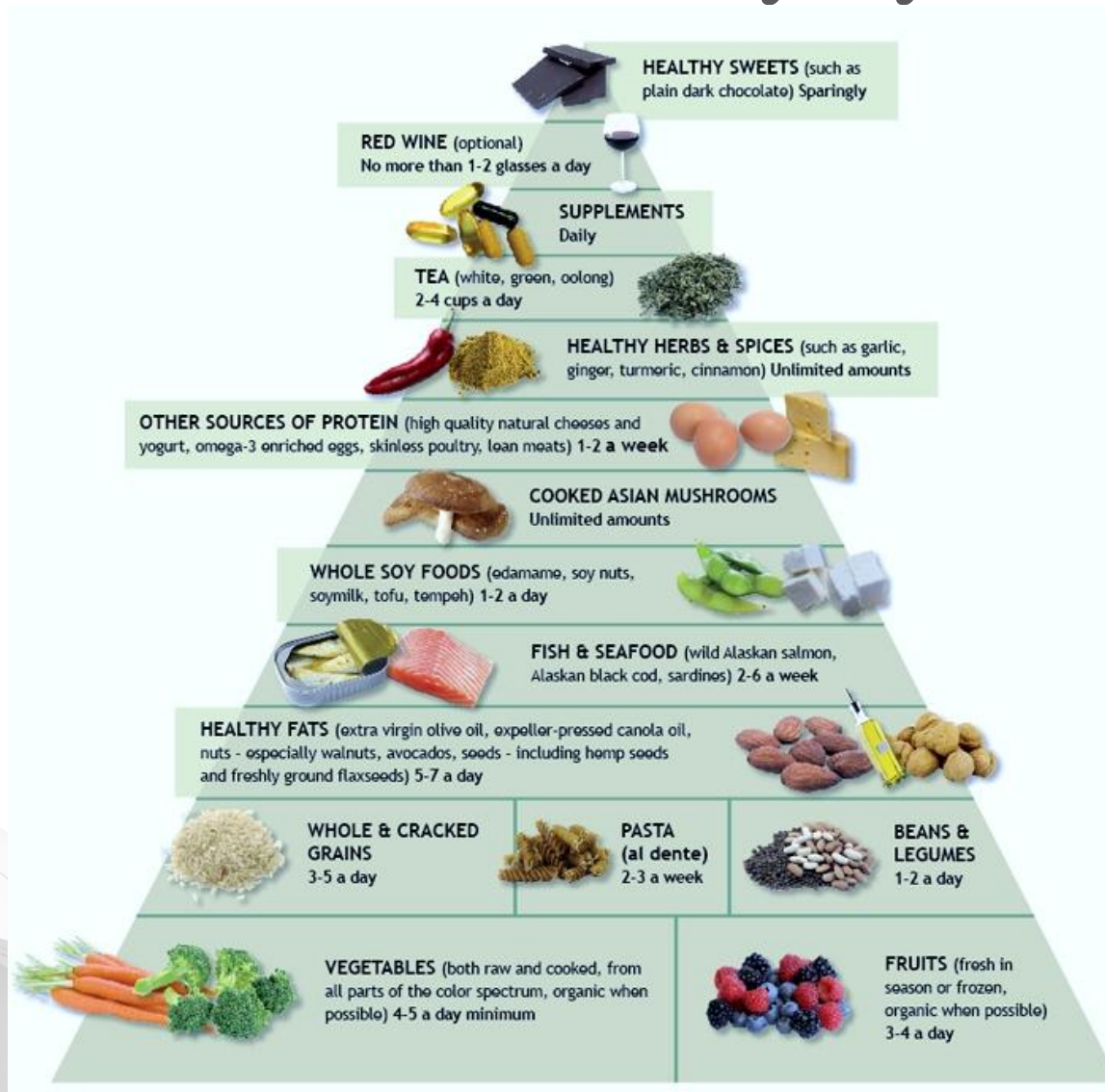
## DNA methylation

# Anti-Inflammatory Diet





# Anti-Inflammatory Pyramid



<b>Food Sources of Chemopreventive Substances</b>	
Phytochemical/ Nutraceutical	Food
<b>Glucosinolates</b>	<b>Broccoli, cauliflower, brussels sprouts, cabbage</b>
<b>Flavonoids</b>	<b>Onions, apples, green/black tea, grapes</b>
Isoflavones	Soy, red clover
<b>Vitamin A</b>	<b>See Carotenoids, important precursors of vitamin A</b>
<b>Vitamin D</b>	<b>Salmon, mackerel, sardines, tuna</b>
Tocopherols/ tocotrienols	Vegetable oils, wheat germ, almonds, rice bran oil, oats, barley, rye
Selenium	Brazil nuts, tuna, cod, eggs
Curcuminoids	Turmeric
Green tea	Green tea
Organosulfurs	Garlic, onions, leeks, green onions, shallots
Flax lignans	Flaxseed
Calcium	Greens, salmon, tofu, broccoli, beans
Carotenoids	Carrots, squash, sweet potatoes, apricots

**Bolded substances are specific to lung cancer**



## Examples of Natural Molecular Target Modifiers

Marker	Nutraceuticals
COX-2	Curcumin, fish oil, ginger, <i>Scutellaria baicalensis</i>
IGF-I	Lycopene, genistein, quercetin
MDR	Rosemary extract, fish oil, indole-3-carbinol
VEGF	Luteolin, apigenin, milk thistle
p53	Green tea (EGCG), genistein
EGFR	Curcumin, resveratrol, grape seed extract
<i>ras</i>	Garlic, limonene, tocotrienols
HER2/neu	Green tea, olive oil
PTEN	Indole-3-carbinol, soy isoflavones

Targeting Progression Pathways with Nutraceuticals									
	Proliferation	Apoptosis	Resistance	Immune	Angiogenesis	Metastasis	Communication	Differentiation	Immortality
Curcumin	X	X	X	X	X	X	X	X	
Green tea polyphenols	X	X	X	X	X	X	X	X	X
Vitamin D	X	X	X		X	X		X	X
Resveratrol	X	X	X	X	X	X	X	X	
Grape seed extract	X	X			X	X			
Reishi	X	X	X	X		X			X
Maitake	X	X		X		X			
Ellagic Acid	X	X	X		X	X		X	
Antho-cyanins	X	X	X		X	X		X	
Luteolin	X	X			X	X		X	

# Telomeres



# UCSF Pilot Study

## Lifestyle Changes May Lengthen Telomeres

A small UCSF pilot study shows for the first time that changes in diet, exercise, stress management and social support can result in longer telomeres, the parts of chromosomes that affect aging.

Here are some lifestyle changes undertaken by study participants:

### 1 DIET



High in whole foods, plant-based protein, fruits, vegetables; Low in fat (10% of calories) and refined carbohydrates

### 2 EXERCISE



Moderate aerobic exercise – walking 30 minutes per day for six days a week

### 3 STRESS MANAGEMENT



Gentle, yoga-based stretching, breathing or meditation for 60 minutes daily

### 4 INCREASED SOCIAL SUPPORT



Weekly support group sessions that included moderate exercise, stress management training and counseling

# Exercise and Lung Cancer Prognosis

- Prospective observational analysis ( $n = 296$ ) of preoperative patients evaluated if performance on stair-climbing test was a prognostic factor in non-small cell lung cancer (NSCLC)
  - Patients who climbed more than 18 meters on the stair climb had *significantly longer* median (months) survival and 5-year survival than those who climbed less than 18 meters (97 vs 74; 77% vs 54%,  $p=0.001$ )
- Interventions aimed at improving exercise tolerance can be useful to improve long-term prognosis after NSCLC operations

# Ketogenic Diet Benefits During Treatment

- One of the fundamental differences between cancer cells and normal cells is in how they break down (metabolize) nutrients to obtain the energy they need to grow and survive
- A ketogenic diet limits glucose metabolism and emphasizes oxidative metabolism of fatty acids, ketone bodies, and amino acids in mitochondria
- Mitochondria from tumor cells produce more superoxide and hydrogen peroxide than mitochondria from normal cells
- Consuming a ketogenic diet should therefore selectively enhance the sensitivity of tumor cells to treatments that increase oxidative stress, such as radiation and chemotherapy



# Ketogenic Diet Benefits During Treatment: Current Clinical Study

- Patients with stage III or IV (with limited metastasis) non-small cell lung cancer will follow a ketogenic diet 48 hours before chemoradiation therapy and continue through the end of the 6- to 7-week treatment period
  - Consume formulated shakes in the morning and work with dietician to maintain similar calorie balance throughout the day
- Assessing:
  - Safety and tolerability of the diet in conjunction with chemoradiation treatment
  - Levels of glucose and ketones in the blood and oxidative stress markers in plasma and urine
- About 90 percent of calories in the ketogenic diet used in the study come from fat, whereas less than 2 percent of calories come from carbohydrates, with protein supplying the remaining calories
- Hypothesis:
  - Ketogenic diet will deprive the tumor of glucose which it depends on for energy as well as enhance oxidative stress

# Foods That *Decrease* Risk of Lung Cancer

- Vegetables/ Leafy Greens
  - A large European study found that consumption of a variety of vegetables is inversely associated with lung cancer risk among current smokers
  - Specifically, leafy greens help reduce risk
- Walnuts
  - The antimutagenic effects of walnut extract were associated with a twofold reduction of mitochondria respiration. These results suggest impairment of mitochondrial function and apoptosis as a relevant mechanism of anticancer effects

# Red Meat as a Trigger

- Milan Cancer Institute Study
  - Patients who consumed red meat 2-3 times weekly had *higher rates of recurrence* than those consuming a Mediterranean diet
- Additional study— lung cancer screening program of over 4000 patients, 178 of whom were diagnosed with lung cancer
  - Found that among heavy smokers, high red meat consumption and low adherence to a Mediterranean diet are associated with *increased risk* of lung cancer

# Other Foods That *Increase* Risk

- Sugar & Saturated Fats
  - Case-control studies of subjects with lung cancer found that high sugar and saturated fat intake increased the risk of lung cancer
- Acrylamide (French fries, potato chips)
  - A large case-cohort study conducted for 13.3 years in The Netherlands found an association between acrylamide intake and lung cancer in women, but no association found in men

# Diet and Exercise Guidelines for Lung Cancer & Resources



# American Cancer Society Guidelines—2006

- Exercise:

- Maintain a healthy weight throughout life
- Balance caloric intake with physical activity

Adults: at least 30 minutes of moderate to vigorous activity on 5 or more days/week; 45-60 minutes better

Children and adolescents: at least 60 minutes of moderate to vigorous activity at least 5 days/week

- Diet:

- Consume a healthy diet, with an emphasis on plant sources
- Eat 5 or more servings of a variety of fruits and vegetables each day; every meal and snacks
- Limit consumption of processed and red meats
- Drink no more than one alcoholic drink per day for women or two per day for men





# Diet Based on Current Research

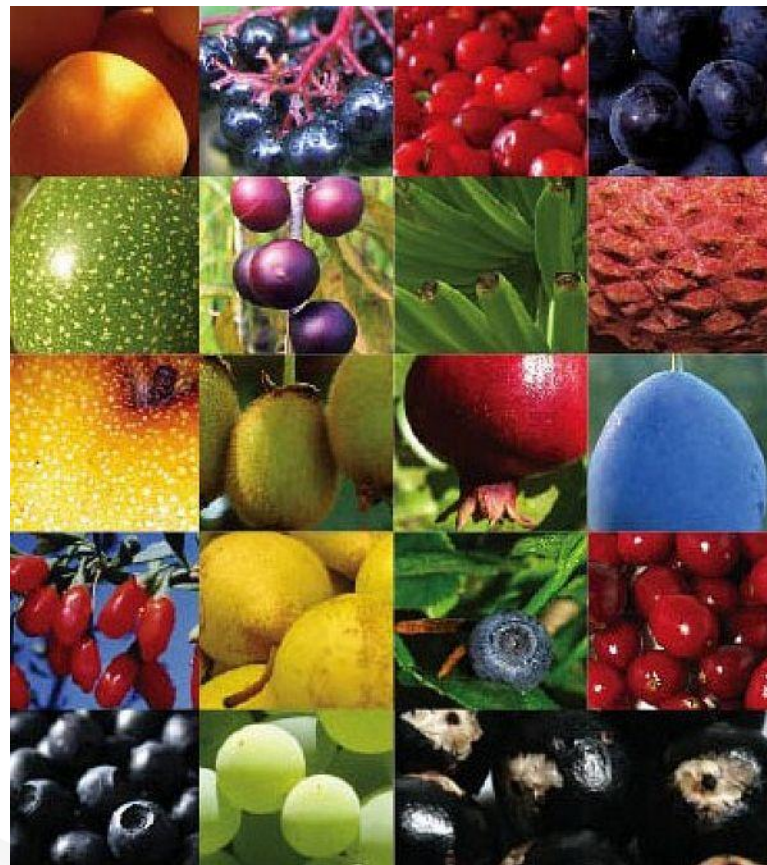
## Encourage

- Mediterranean Diet
- Anti-Inflammatory Diet
- Regular consumption of green leafy vegetables and Brassica vegetables
- Regular consumption of nuts (e.g. walnuts), seeds, fruits, and spices

## Avoid

- Foods rich in simple carbohydrates and saturated fats
- Foods rich in acrylamide, including heated starches such as fried or baked potato products (French fries, potato chips) and coffee

# Antioxidants



# My Antioxidant Approach

- Individual advice depends on goal of Rx
  - If cure, err on side of caution
    - Delay antioxidants until end of Rx
    - Discontinue day before, of, after chemo cycle
    - Antioxidant rich foods probably ok
  - If palliation, encourage use for protection of normal tissue, optimization of QOL
- Antioxidant radio- and chemoprotectants (mesna, amifostine) do not interfere with anti-tumor effects of Rx

# Resources for More Information

- National Cancer Institute
  - [www.cancer.gov](http://www.cancer.gov) - Information about cancer causes and prevention, screening and diagnosis, treatment and survivorship; clinical trials; statistics; and more
  - <http://livehelp.cancer.gov> - Instant messaging service for cancer information
  - 1-800-4-CANCER (1-800-422-6237) – Toll-free cancer Information Service provided in English and Spanish
- National Center for Complementary & Alternative Medicine
  - <http://nccam.nih.gov/health/cancer/camcancer.htm>
- Anti-Inflammatory Diet
  - [www.drweil.com](http://www.drweil.com)

Thank you!

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