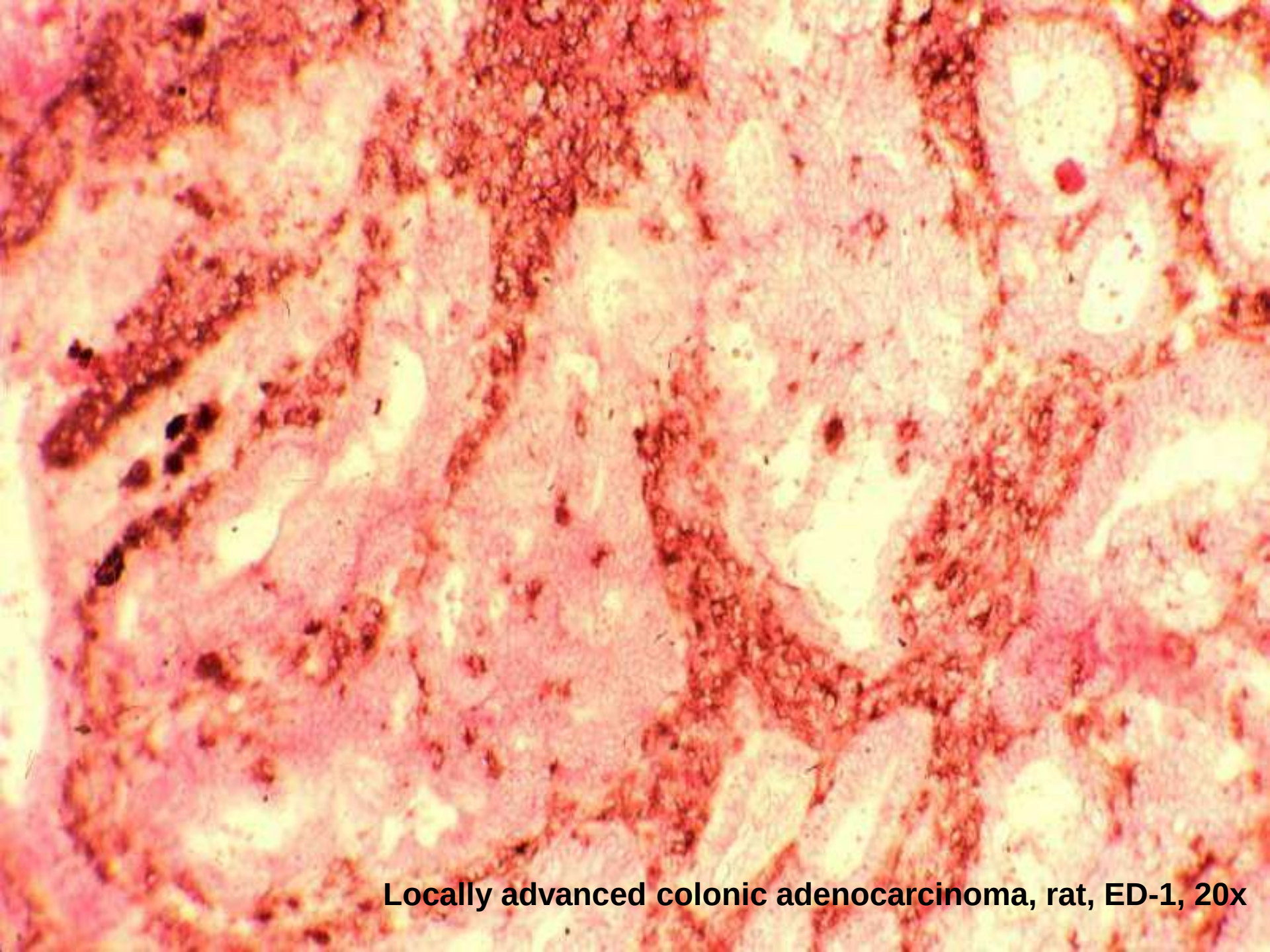
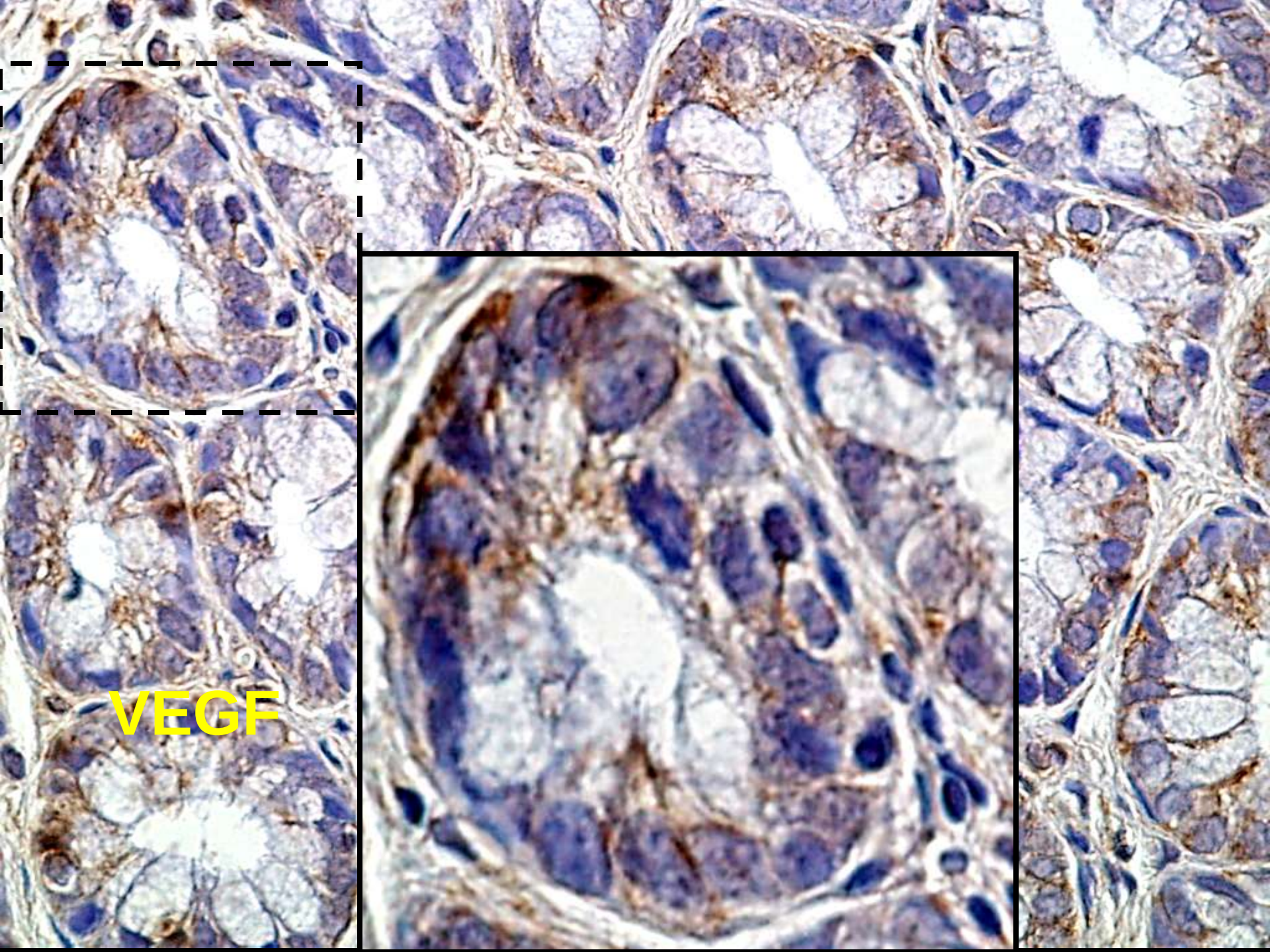
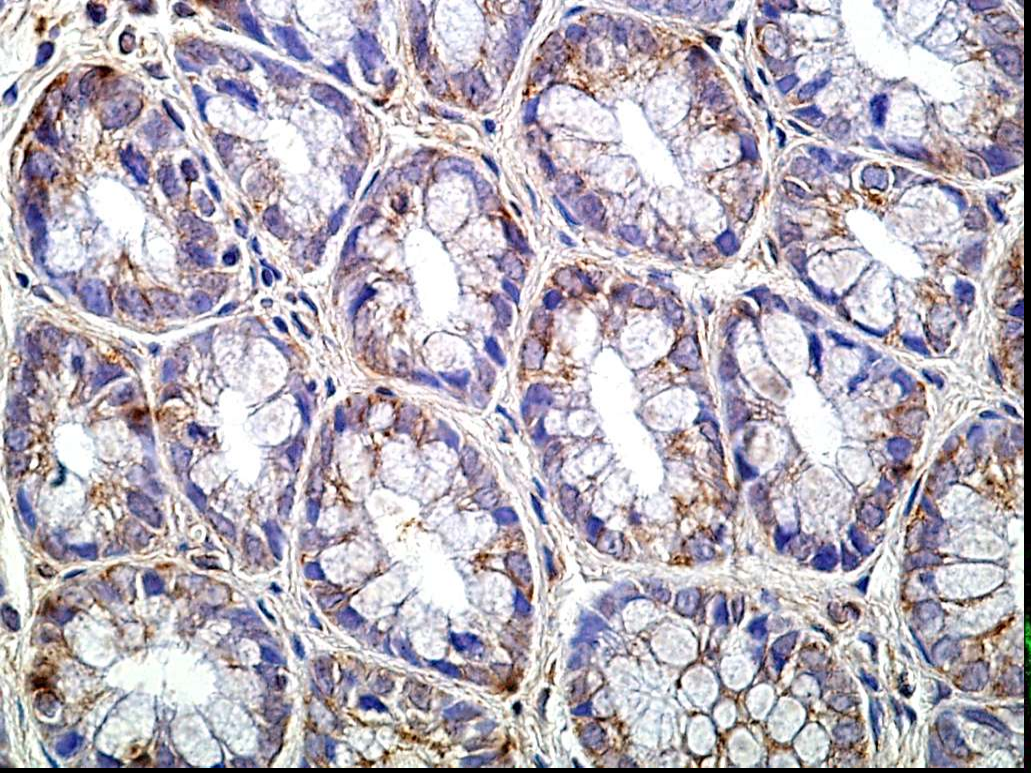


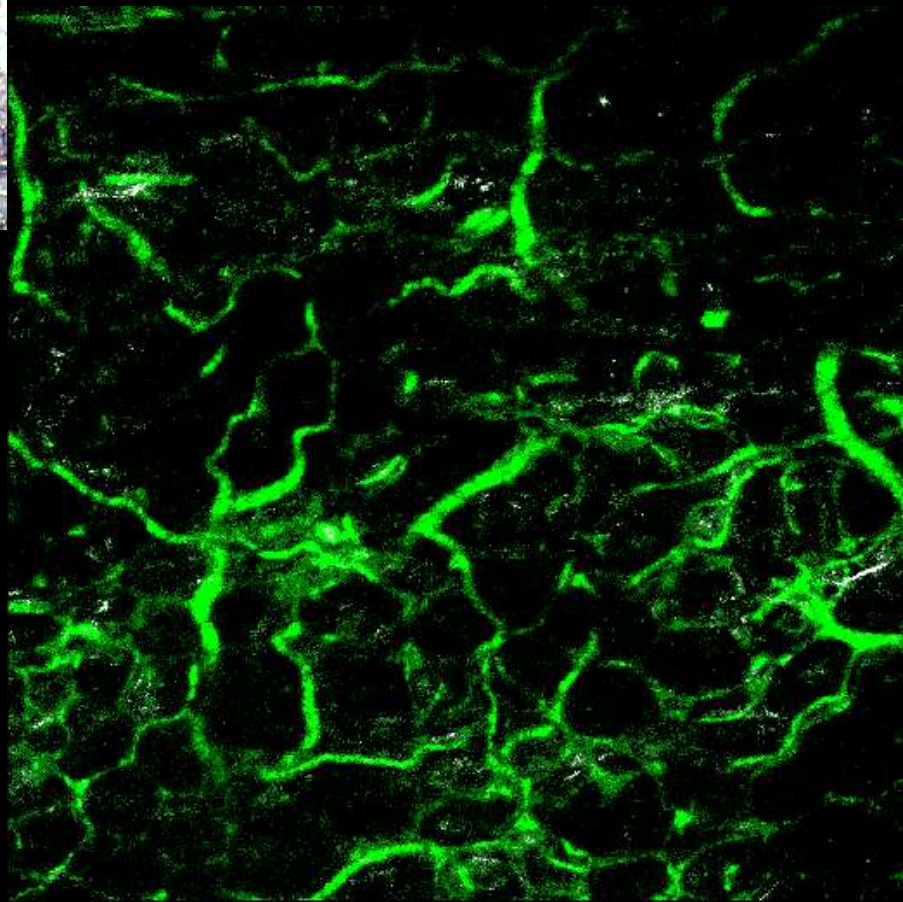
Locally advanced colonic adenocarcinoma, rat, ED-1, 20x


VEGF



VEGF expression in colonic mucosa during experimental carcinogenesis

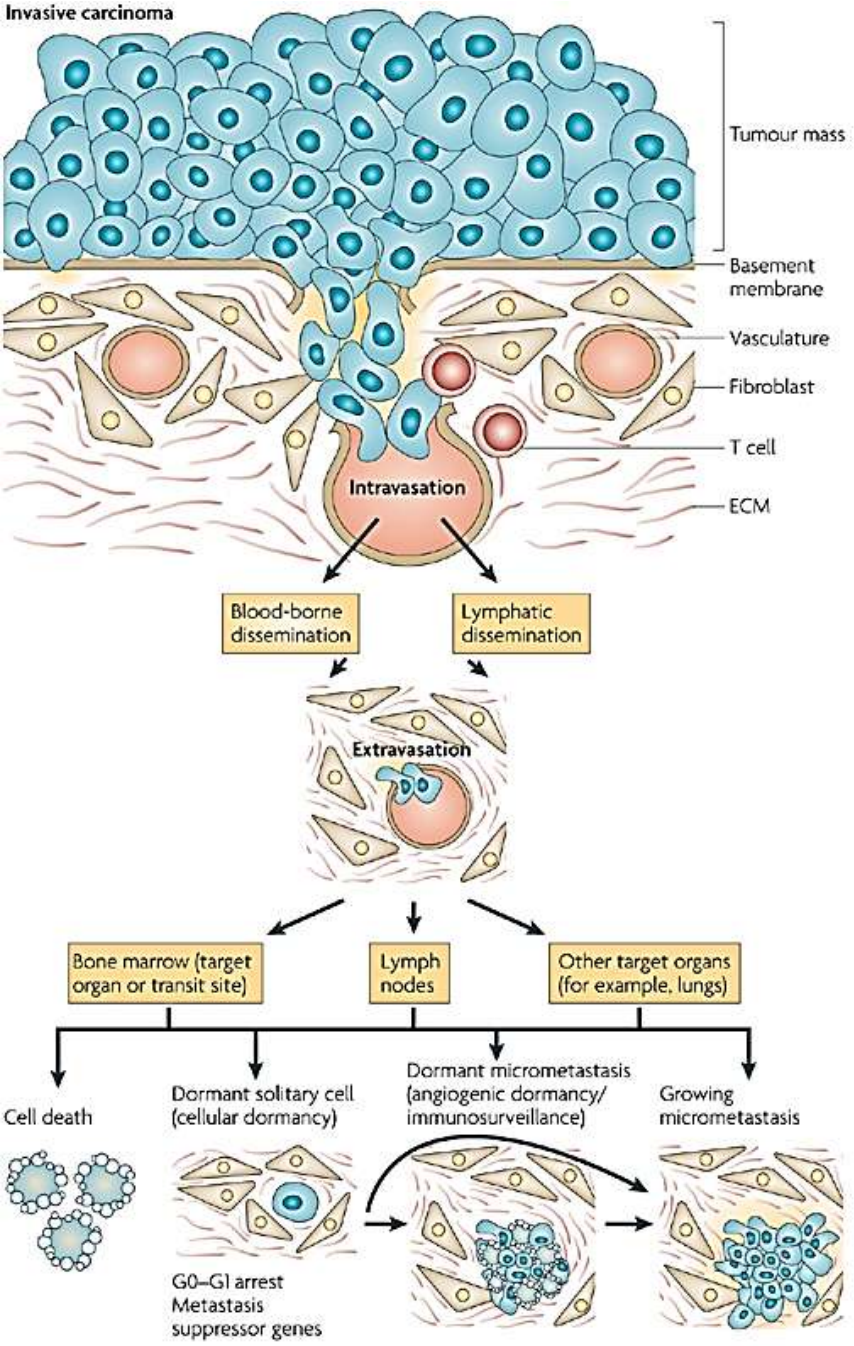
immunohystochemistry, 40x magn.



Neo-angiogenesis at the basement of a colonic tumor in the rat after experimental carcinogenesis with AOM+bile

(Vannucci et al., Int J Onc, 2004)

confocal microscopy after in vivo injection of dextran-FITC, 20x magn



Nature Reviews | Cancer

FOOD AND CANCERS

Breast cancer

The risk of breast cancer in women is increased by several factors that cannot be easily changed:

- Having your first period before age 12
- Not having children or having your first child after age 30
- Late age at menopause
- Family history of breast cancer

Both **increased body weight and weight gain** as an adult are linked with a **higher risk of breast cancer after menopause** (disbalance of fat metabolisms may affect hormonal production).

Even low levels of **alcohol intake** have been linked with an increase in risk.

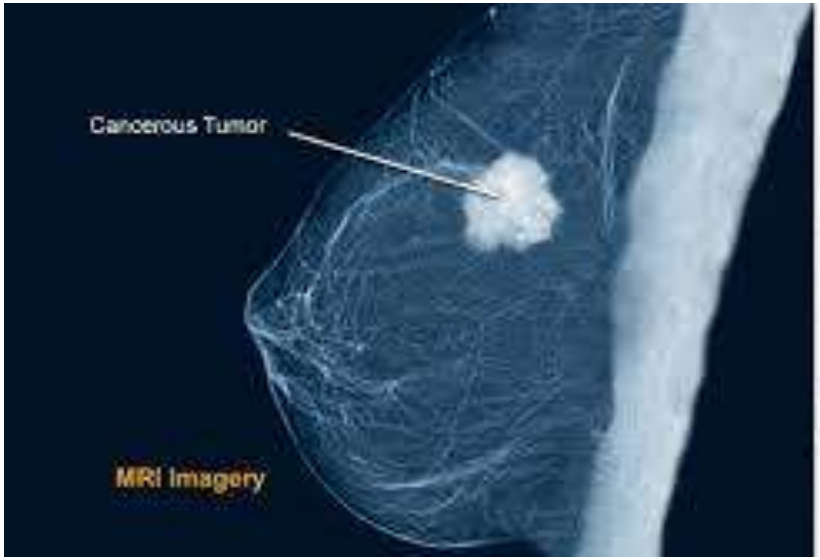
Not clear if specific vegetables, fruits, or other foods can lower risk.

Recommendations:

Get regular, **intentional physical activity.**

Reduce lifetime weight gain by limiting your calories and getting regular physical activity.

Avoid or limit your alcohol intake.



Colorectal cancer

Higher risk of colorectal cancer is for those with:

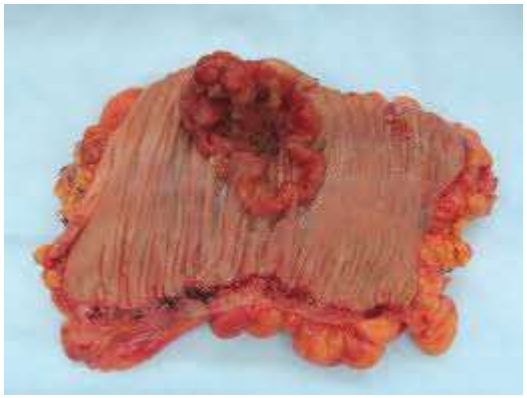
- **relatives** who have had colorectal cancer or polyps
- **long-term tobacco use** and excessive **alcohol use**

Diets that are **high in vegetables, fruits, and whole grains** (and **low in red and processed meats**) have been linked with lower colorectal cancer risk, although it's not exactly clear which factors are important.

Many studies have found a **link between red meat or processed meat intake** and colorectal cancer risk.
Lower risk of colorectal cancer and polyps with **increasing levels of activity.** Moderate activity on a regular basis lowers the risk, but vigorous activity may have an even greater benefit.
Fiber intake, especially from whole grains, may lower colorectal cancer risk

Calcium, vitamin D, or a combination of the two may help protect against colorectal cancer

HOWEVER possible **increased risk of prostate cancer in men with high calcium intake**



Recommendations:

Increase the intensity and amount of physical activity.

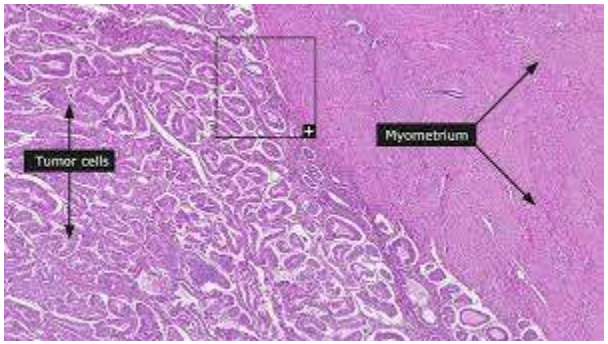
- Limit intake of red and processed meats.
- Get the recommended levels of calcium and vitamin D.
- **Eat more vegetables and fruits**.
- **Avoid obesity and weight gain** around the midsection.
- **Avoid excess alcohol**.

Regular colorectal screening :
Occult blood in the feces
Endoscopy if familiarity

Endometrial (uterine) cancer

A link between **a higher risk** of endometrial cancer (cancer of the lining of the uterus) and being **overweight or obese** , having more belly fat (that is, a **larger waistline –risk from 90 cm**) that looks to correlate with **increase in estrogen levels** that happens when women are overweight.
Spending **more time sitting** (regardless of overall activity level) has also been linked with a higher risk.

Lower risk with high physical activity levels, although in some studies this has been limited to women who are overweight or who have not yet gone through menopause.



Vegetable and fiber intake may lower risk, although some studies have not found this. The evidence for red meat, saturated fat, animal fat, and alcohol raising risk is also conflicting among different studies.

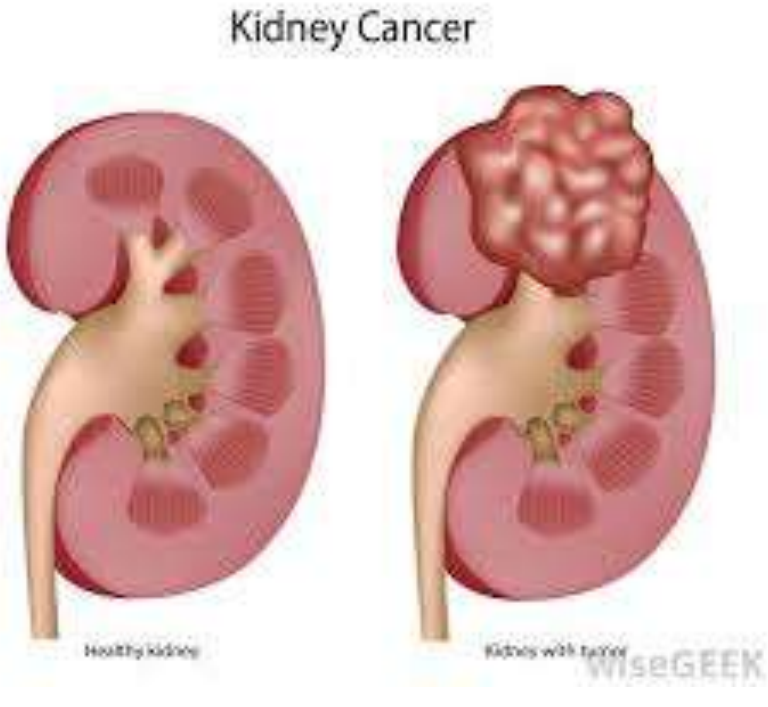
At this time, the best advice about diet and activity to possibly lower the risk of endometrial cancer is to get to and stay at a **healthy weight and to get regular physical activity**

Kidney cancer

The causes of kidney cancer are not clear, but the best-known risk factors that can be changed are **obesity** and **tobacco smoking.**

Studies looking for links between specific parts of the **diet and kidney cancer have not shown clear results**. A small number of studies have found a possible link between **physical activity** and lowered risk of kidney cancer.

The best advice to possibly lower risk for kidney cancer is to stay at a **healthy weight and avoid tobacco use.**



Lung cancer

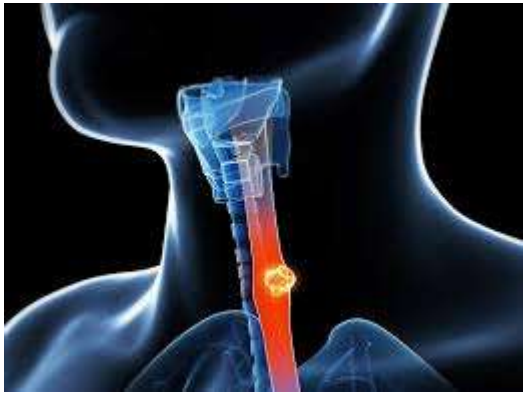
More than **85%** of lung cancers result from **tobacco smoking,** but other factors, such as **radon exposure**, are also linked to lung cancer.

Many studies have shown that the risk of lung cancer is lower among both smokers and non-smokers who **eat at least 5 servings of vegetables and fruits a day**. Although healthful eating may reduce the risk of lung cancer, the risks from tobacco remain high. Using **high-dose beta-carotene and/or vitamin A supplements has been shown to increase** (not decrease) **lung cancer risk among smokers**

The best advice to reduce the risk of lung cancer is **to avoid tobacco use** and secondhand smoke and to avoid **radon exposure**.
According to Chines studies also **fumes from high-temperature oils** may increase the risk after repeated expositions.

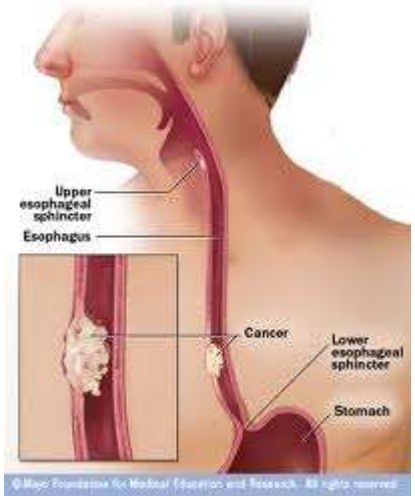
Mouth, throat, and esophagus cancers

Tobacco (including cigarettes, chewing tobacco, and snuff), **alcohol**, and especially **the combination of the two**, increase the risk for cancers of the mouth, larynx (voice box), pharynx (throat), and esophagus.



Obesity raises the risk for **cancer in the lower esophagus** and at the **junction of the esophagus and stomach** (likely due to increased acid reflux). **Very hot beverages and foods** may also increase the risk of **mouth and esophagus cancers**, likely as a result of the damage heat can cause.

A **diet high in vegetables and fruits may reduce the risk** of mouth and esophagus cancers.



The best advice to possibly reduce the risk of these cancers is to:

- Avoid all forms of tobacco.
- Restrict alcohol intake.
- Avoid obesity.
- Eat at least 2½ cups of vegetables and fruits each day.

Ovarian cancer

The causes of ovarian cancer are not well understood. **Family history** is a risk factor, but only **about 10% of ovarian cancers are inherited**.

There are **no clearly proven nutritional risk factors for ovarian cancer**. Some studies have found that **obesity** may increase the risk for ovarian cancer, as may a **diet high in fat (especially saturated fat**). The role of physical activity in ovarian cancer risk is unclear. Studies of vegetables, fruits, meat, dairy products, and alcohol have not found clear links.

Some studies have found possible role for **eating soy foods and drinking tea (especially green tea)** in lowering ovarian cancer risk, but not all studies have found this, therefore controversial.

At this time, it is **not clear how nutrition and physical activity might be related to ovarian cancer risk,** so no strong recommendations can be made.

Pancreatic cancer

Tobacco smoking, **type 2 diabetes**, and **impaired glucose tolerance** ("borderline diabetes"), **chronic pancreatitis** all increase the risk for pancreatic cancer.

A link between being **overweight or obese** and having a higher risk of pancreatic cancer. Also a link between having more belly fat (that is, a **larger waistline**) and pancreatic cancer, especially in women.

Pancreatic cancer **risk may be reduced** with **higher levels of physical activity**. On the other hand, **diets high in red and processed meats and low in fruits and vegetables have been linked with increased risk** in some studies. It is needed to confirm these findings.

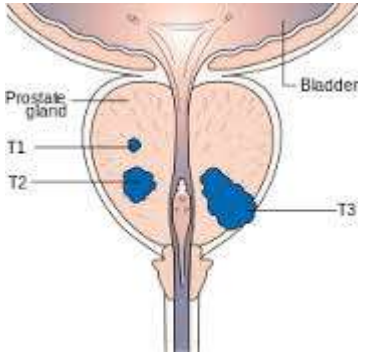
Possible links with **alcohol intake ..**

The best advice is to **avoid tobacco use** and stay at a **healthy weight**. Being **physically activ**e and following the other ACS recommendations related to a **healthy diet** may also be helpful.

Prostate cancer

Related to **age**, **family history**, and **male sex hormones**, but just how diet and activity factors might affect risk is not clear.

Men who are overweight may have a **lower risk of prostate cancer overall**, but **more aggressive cancer when it develops**. **Being overweight affects also treatment, worsening the prognosis.**
Regular physical activity slightly lowers risk of prostate cancer. **Vigorous activity may have a greater effect**, especially on the risk of advanced prostate cancer.



Diets high in certain vegetables (including **tomatoes, cruciferous vegetables, soy, beans, and other legumes**) or **fish** may lower the risk of more advanced cancers.

No benefit from supplements containing antioxidant nutrients, such as vitamin E or selenium. Eventually vit. E might raise prostate cancer risk slightly. Diets high in **calcium** may **raise prostate cancer risk**. **Dairy foods may also increase risk (calcium)**.

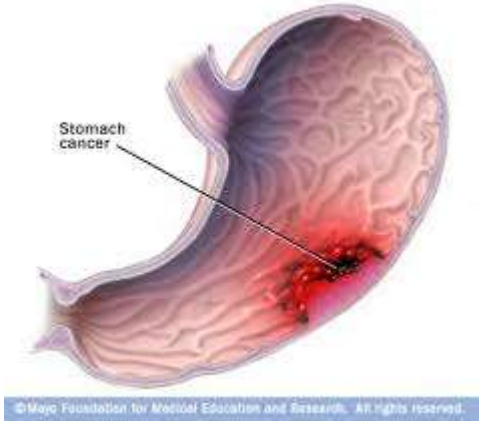
Advice about diet and activity :
- Eat at least 2½ cups of **a wide variety of vegetables and fruits each day.**
- **Be physically active**.
- Stay at a **healthy weight**
- **limit calcium supplements as well as in the diet.**

Stomach cancer

Stomach cancer cases in most parts of the world are diminishing. While stomach cancer is fairly rare in the United States, the rate of **cancers in the first part of the stomach (the cardia**) has risen in recent years. This may be due at least in part to increases in **gastric reflux, which has been linked to obesity**.

High intake of fresh fruits and vegetables is lowering risk of stomach cancer, while **a high intake of salt, salt-preserved foods, and possibly processed meat increase the risk**.

Increased risk with higher body weight. There are also few studies that have looked at the effects of physical activity on stomach cancer, but it seems to be linked with a lower risk.



Advice to possibly reduce the risk of stomach cancer is to:

- **Eat at least 2½ cups of vegetables and fruits daily**.
- **Reduce** intake of processed **meat, salt, and foods preserved with salt.**
- Be **physically active.**
- Stay at a **healthy weight.**

Last Revised: 04/09/2015

http://www.cancer.org/healthy/eathealthygetactive/acsguidelinesonnutritionphysicalactivityforcancerprevention/acs-guidelines-on-nutrition-and-physical-activity-for-cancer-prevention-dietand-activity

Conclusions:

Relations between food and cancer are present.

Type of alimentary attitude can influence microbiota, immunity, metabolism and general physiology of the organism

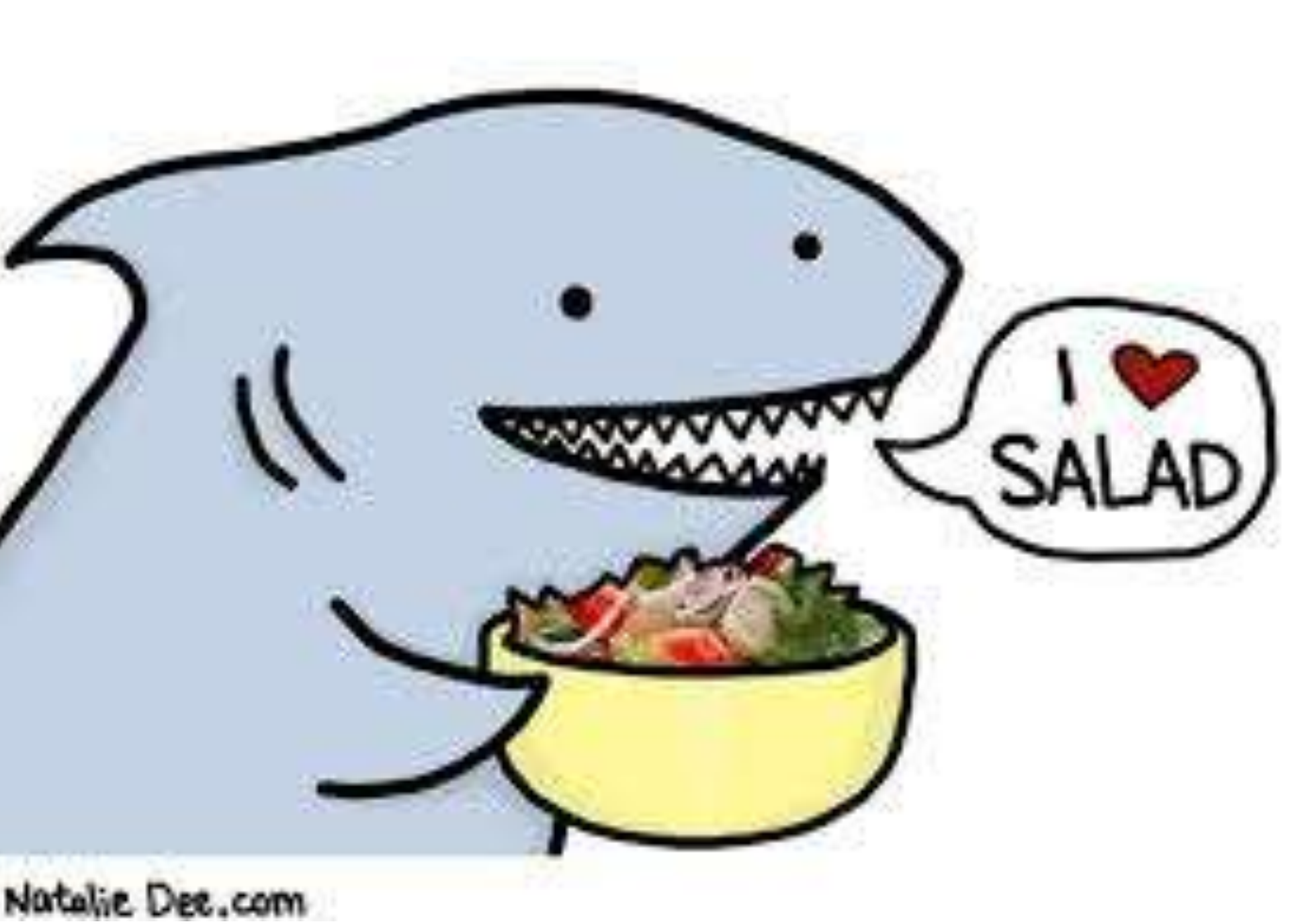
The classic Western diet cannot be used as the standard diet because obesity risk, cardiovascular risks and cancer risks
Microbiota modulation by probiotis is a new opportunity

It is recommended:

Physical activity

Weight control

Fresh vegetables, fruit and fibers (prebiotics), probiotics

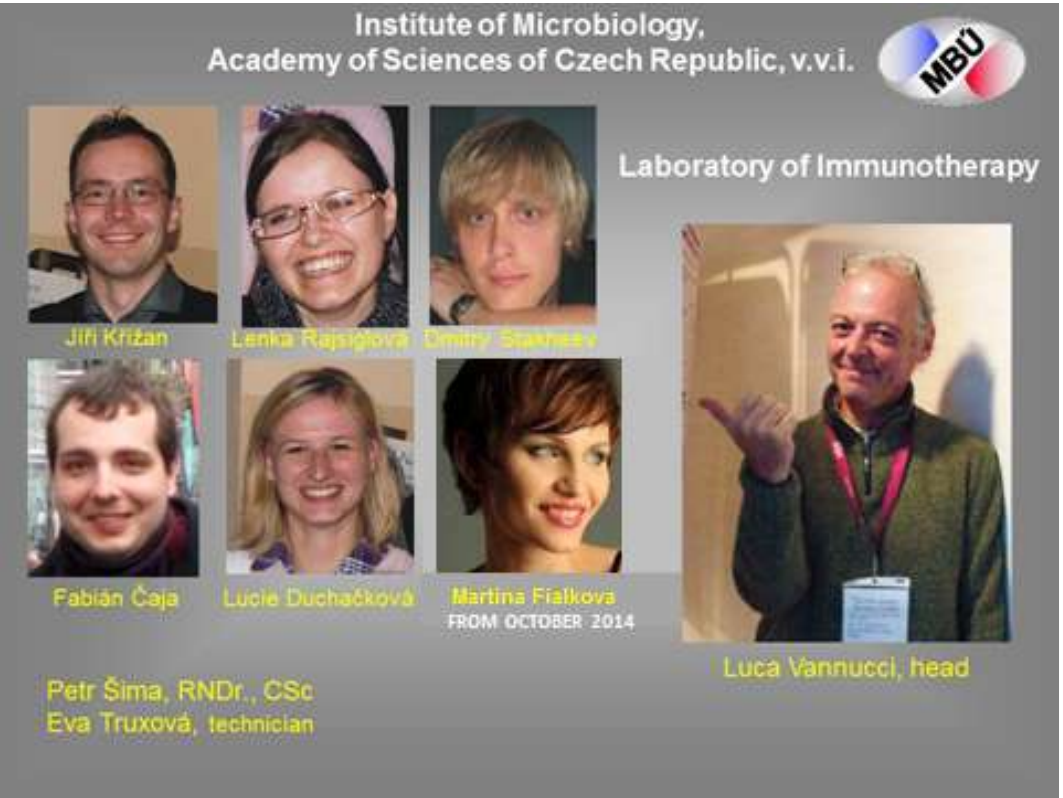

I ♥ SALAD
Natalie Dee.com

vannucci@biomed.cas.cz

Laboratory of Immunotherapy

Institute of Microbiology , ASCR, v.v.i.

Videnska 1083 – PRAGUE 4 Krc



Laboratory of Gnotobiology
R. Stepankova
H. Kozakova
T. Hudcovic

Laboratory of Cellular and Molecular Immunology
H. Tlaskalova-Hogenova
M. Kverka
P. Rossmann

Dept. of Biomathematics Institute of Physiology, ASCR, v.v.i.
O. Chernyavskiy
L. Kubinova

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GRANT IAA500200917 (CZ)

THANK YOU FOR ATTENTION

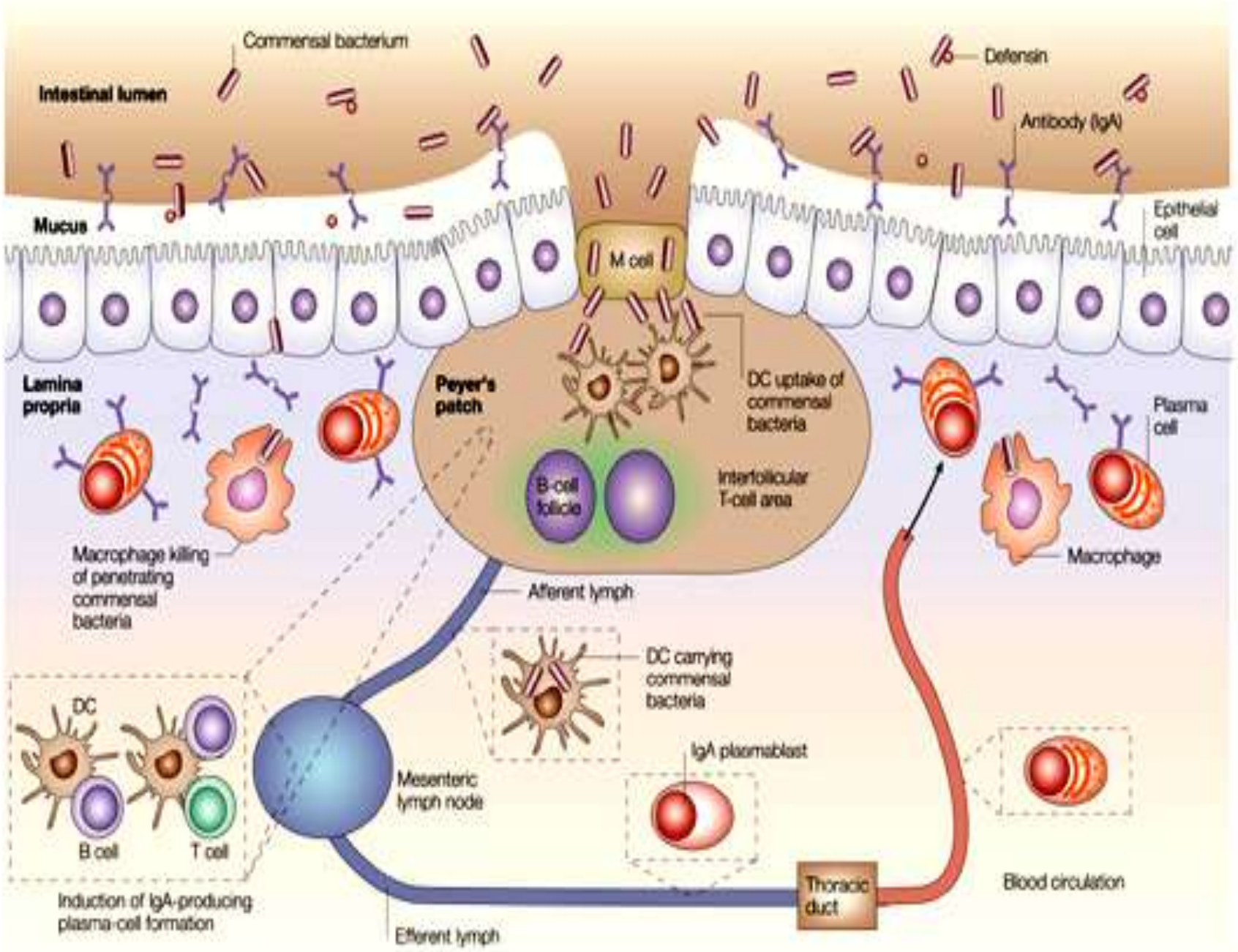
Irradiated foods

Irradiation of food products is one way to limit the risk of germ contamination and food poisoning. In the United States, some foods, such as spices, are routinely irradiated. Irradiated meats and other foods are also widely available. Because radiation is known to cause cancer, there has been concern that food irradiation may present a cancer risk. However, radiation does not remain in foods that have been irradiated.

Prebiotics are nondigestible carbohydrates that act as food for probiotics. When probiotics and prebiotics are combined, they form a synbiotic. Fermented dairy products, such as yogurt and kefir, are considered synbiotic because they contain live bacteria and the fuel they need to thrive.

Probiotics are found in foods such as yogurt, while prebiotics are found in whole grains, bananas, onions, garlic, honey and artichokes.


tomatoes
artichokes
onions
garlic
chicory
dandelion greens
asparagus
leeks
Foods Naturally High in Prebiotics
www.exhibithealth.com
berries
bananas
flax seed
legumes



Nature Reviews Immunology **4**, 478-485 (June 2004) | doi:10.1038/nri1373

OPINION: Interactions between commensal intestinal bacteria and the immune system

Andrew J. Macpherson[1] and Nicola L. Harris[1]

GUT MICROBIOTA

10^{13} -10^{14} microbes

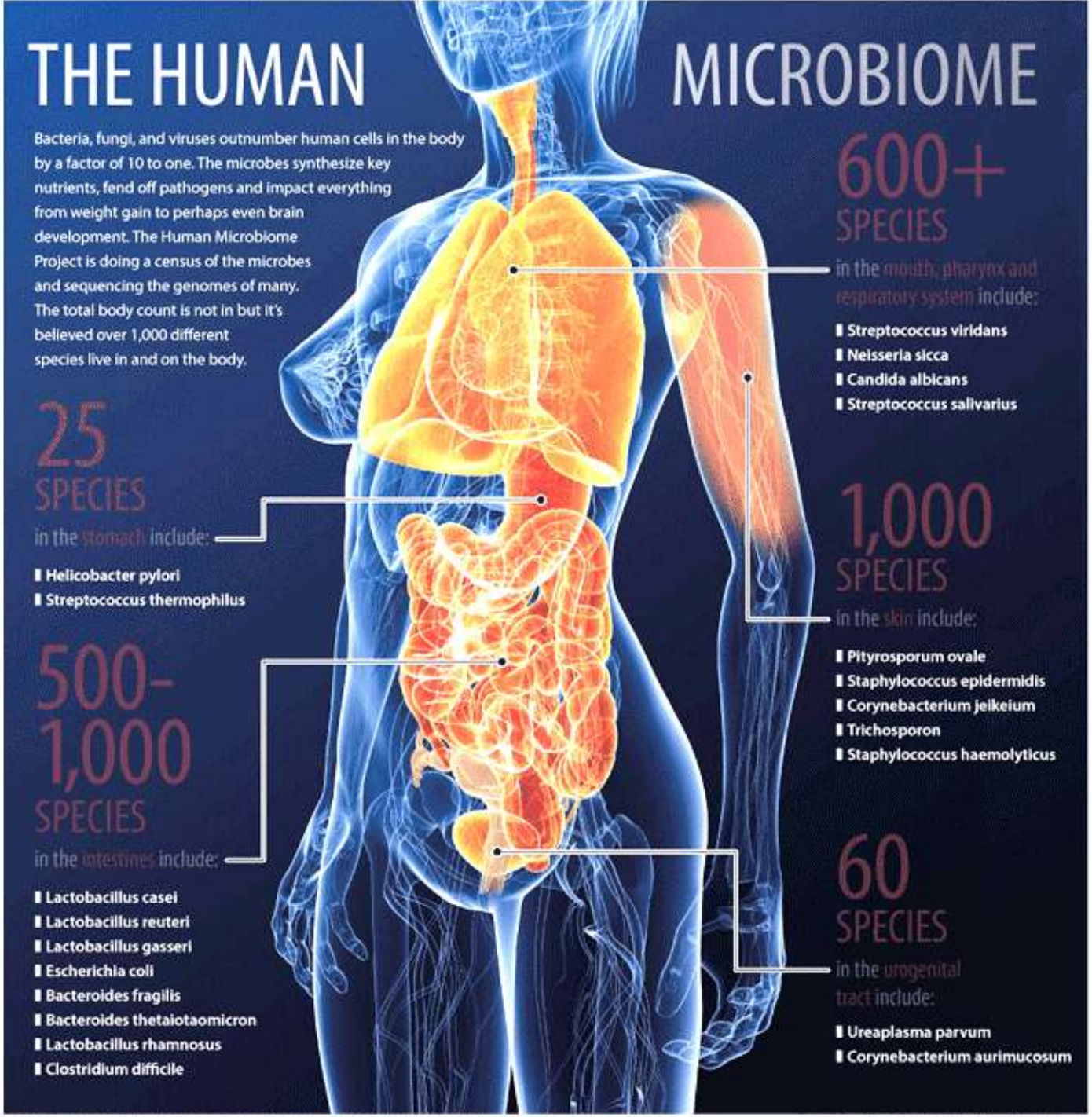
1000- 35000 of species (most of them are still to be identified)

Weight – **3 to 5 lbs**

Genome – **150 fold of our Genome**

Bacteroides, Prevotella, Fusobacterium, Eubacterium, Ruminococcus, Peptococcus, Peptostreptococcus, Bifidobacterium.
***Escherichia* and *Lactobacillus*.**

Bacteroides alone constitute about 30% of all bacteria in the gut.....



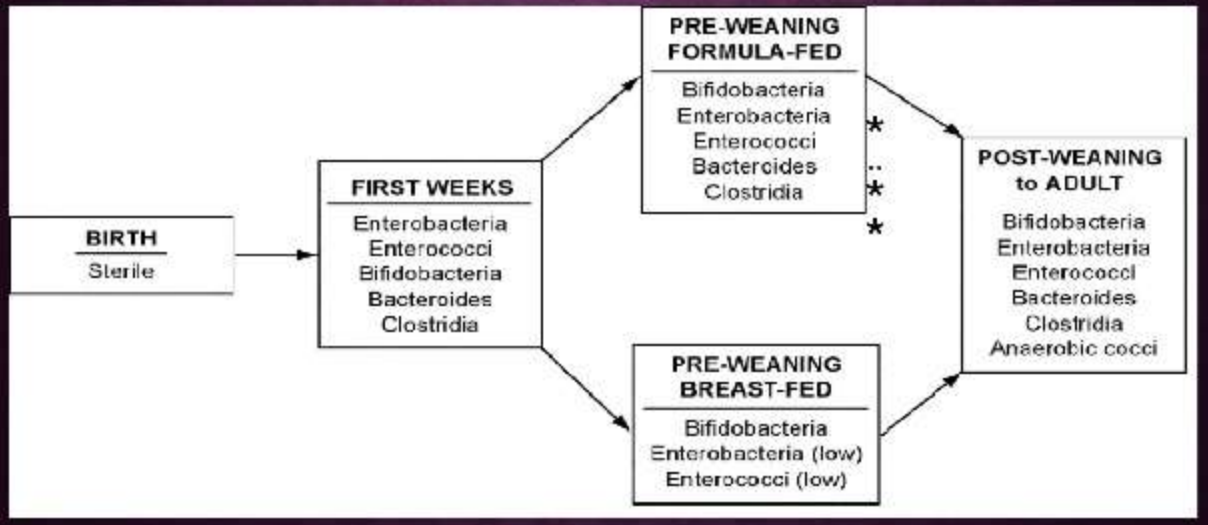
We have about 10 times as many microbial cells as human cells.

The human microbiota consists of the 10-100 trillion symbiotic microbial cells harbored by each person,

primarily bacteria in the gut

Lina.et,al 2012

Primary Succesion in the Human Gut



- Stereotypical succession: suggests that

The gut environment selects its microbiota

TABLE 2 Predominant Bacterial Phyla in the Human Body

Phylum	Class	Characteristics	Examples
Firmicutes	Bacilli; Clostridia	Gram-positive; diverse in their morphology (rod, coccoid, spiral), physiology (anaerobic, aerobic); include commensal and beneficial bacteria	*Lactobacillus*; *Ruminococcus*; *Clostridium*; *Staphylococcus*; *Enterococcus*; *Faecalibacterium*
Bacteroidetes	Bacteroidetes	Gram-negative; composed of 3 large classes widely distributed in the environment, including soil, seawater, and guts of animals	*Bacteroides*; *Prevotella*
Proteobacteria	Gammaproteobacteria; Betaproteobacteria	Gram-negative; include a wide variety of pathogens	*Escherichia*; *Pseudomonas*
Actinobacteria	Actinobacteria	Gram-positive; diverse morphology; major antibiotic producers in the pharmaceutical industry	*Bifidobacterium*; *Streptomyces*; *Nocardia*

Johnson, Pediatrics, 2012

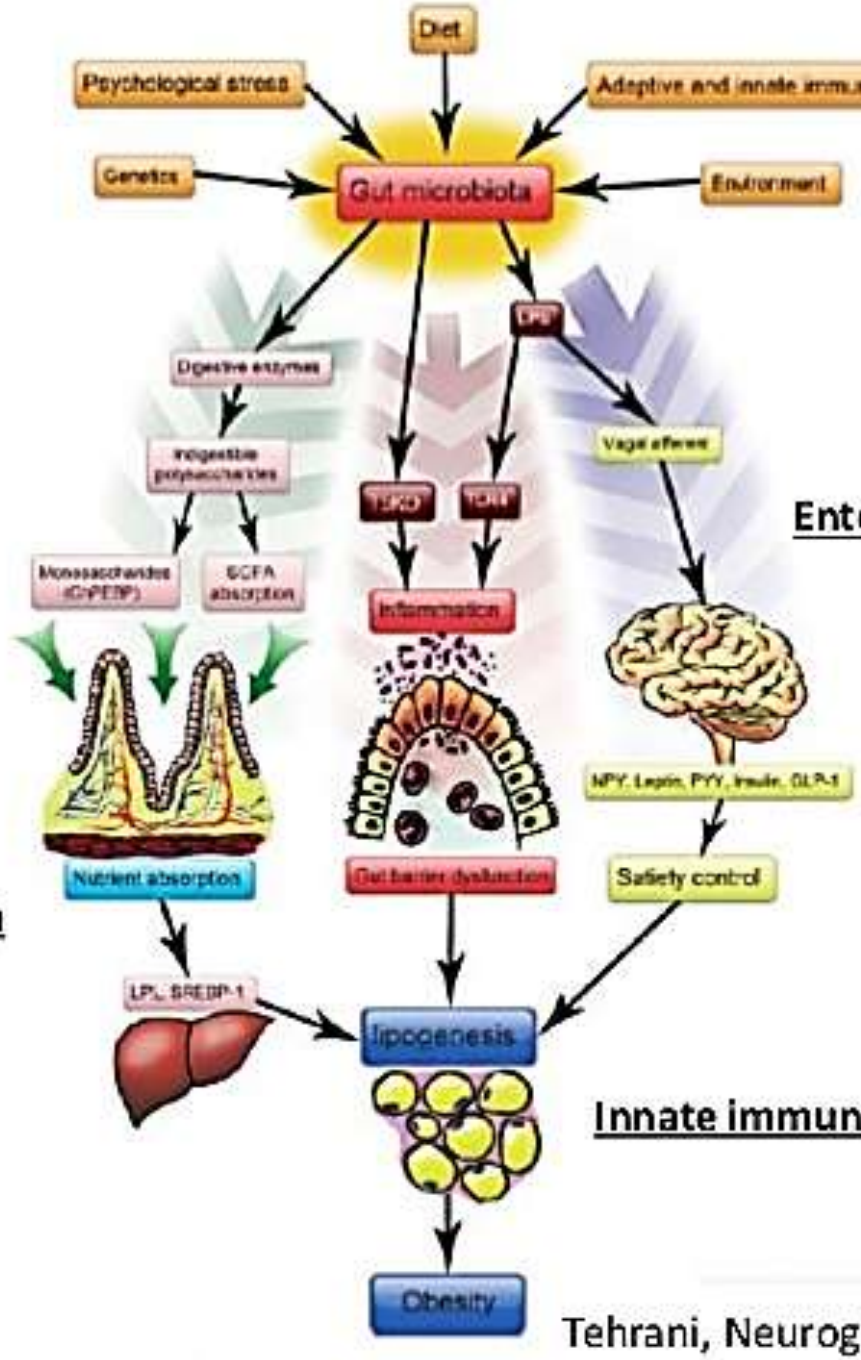
Early Influences on Microbiota

- Gestational age
- Mode of birth (vaginal vs. c-section)
- Maternal microbiome
- Exposure to environment (city vs. farm)
- Diet including breast milk vs. formula
- Hospitalization and use of antibiotics

KOALA Birth Cohort Study

- C/S infants have lower bifidobacteria and baceteroides and more C difficile.
- Bifido and bacteroides may be protective against obesity.

Reinhardt, JPGN, 2009



Enteroendocrine

Peripheral metabolism

Innate immune system

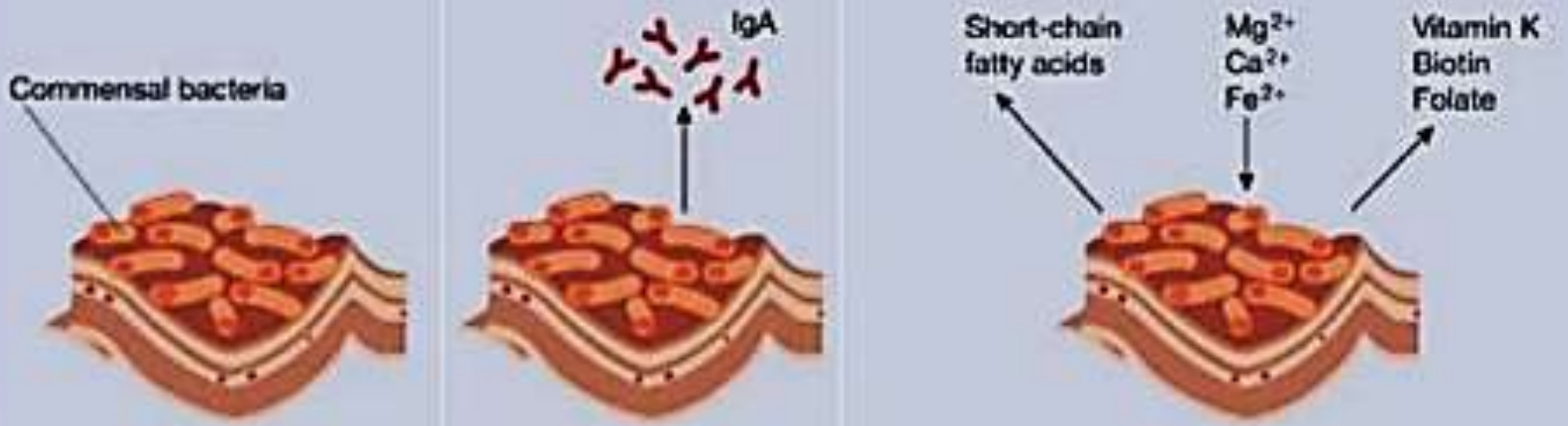
Tehrani, Neurogastroenterol Motil, 2012

THE MICROBIOME: WHO'S THERE?

- Adult Microbiome:
  - Increasing diversity of flora as we age
  - In some newer PCR (16S rRNA) studies, up to 92% of the flora in adults were "novel" species
  - Serial stool collections show remarkable stability by an individual
    - Greatest concordance with twins
    - Less concordance with households
    - Host genetic influence unexplored.

McCartney and Gibson in Gastrointestinal Microbiology, 51-73, 2006

Protective functions	Structural functions	Metabolic functions	
Pathogen displacement	Barrier fortification	Control IEC differentiation and proliferation	Ferment non-digestible dietary residue and endogenous epithelial-derived mucus
Nutrient competition	Induction of IgA	Metabolize dietary carcinogens	Ion absorption
Receptor competition	Apical tightening of tight junctions	Synthesize vitamins e.g., biotin, folate	Salvage of energy
Production of anti-microbial factors e.g., bacteriocins, lactic acids	Immune system development		



O'Hara, EMBO, 2006

THE MICROBIOME: WHO'S THERE?

- Early gut colonization has four phases
  - Phase 1: Sterile gut
  - Phase 2: Initial acquisition: vagina, feces, hospital
  - Phase 3: Breast feeding or bottle-feeding (different)
    - Breast fed more bifidobacteria (up to 90% of flora)
    - Bottle fed more diverse; more *Bacteroides* , and Clostridial species
  - Phase 4: Start of solids; move to adult flora
    - Bifidobacteria remain key flora into adulthood

Ley, Peterson, Gordon. Cell 2006 ;124:837
Ley, et al. PNAS. 2005, 102: 11070
Edwards, et al. Br J Nutr. 2002

TUMOR MICROENVIRONMENT AND TUMOR DEVELOPMENTAL NICHES

CELLS	Normal tissue cells (all tissue components)
	Transformed cells
	Immune cells
PRODUCTS	Secreted biologically active molecules
	Products of metabolism/degradation
	Components of necrotic/apoptotic cells
STRUCTURES	Original tissue
	Vascular net (including lymphatics)
	Nerves
	Stromal fibers

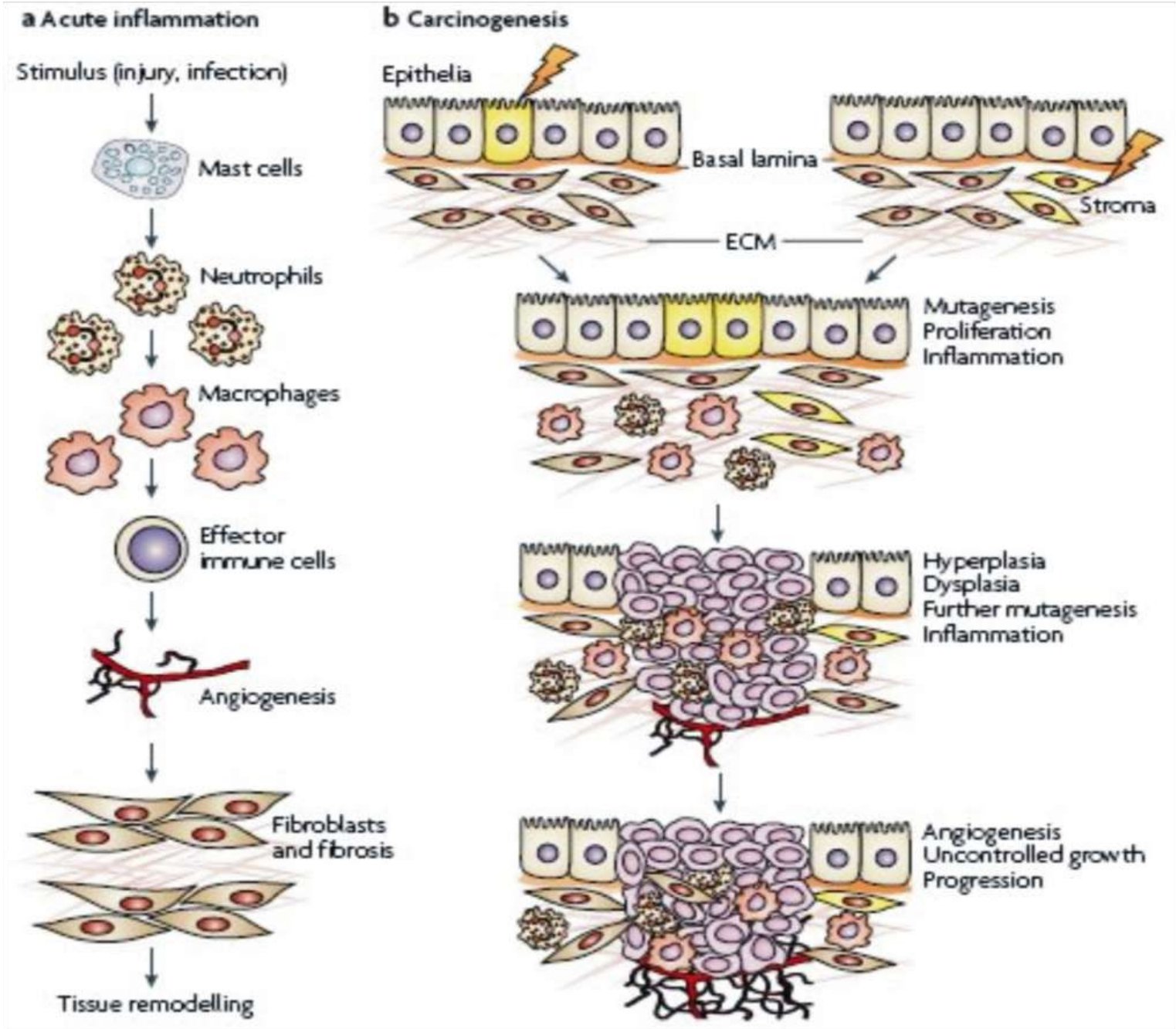
Sonnenschein C, Soto AM. Theories of carcinogenesis: an emerging perspective. Semin Cancer Biol. 2008 Oct;18(5):372-7.

the TOFT model

The **tissue organization field theory** (TOFT). Its premises are significantly different from those of the SMT (somatic mutation theory) namely

- carcinogenesis is a problem of tissue organization, comparable to organogenesis during early development
- *proliferation is the default state* of all cells

- Therefore, cell proliferation control can depend from the tissue organization



www.migration.wordpress.com/.../.

used to boost the immune system in people whose body defenses have been weakened by conditions such as chronic fatigue syndrome, or physical and emotional stress; or by treatments such as radiation or chemotherapy. Beta glucans are also used for colds (common cold), flu (influenza), H1N1 (swine) flu, allergies, hepatitis, Lyme disease, asthma, ear infections, aging, ulcerative colitis and Crohn's disease, fibromyalgia, rheumatoid arthritis, and multiple sclerosis.

People apply beta glucans to the skin for dermatitis, eczema, wrinkles, bedsores, wounds, burns, diabetic ulcers, and radiation burns.

Healthcare providers sometimes give beta glucans by IV (intravenously) or by injection into the muscle to treat cancer and to boost the immune system in people with HIV/AIDS and related conditions. Beta glucans are also given by IV to prevent infection in people after surgery.

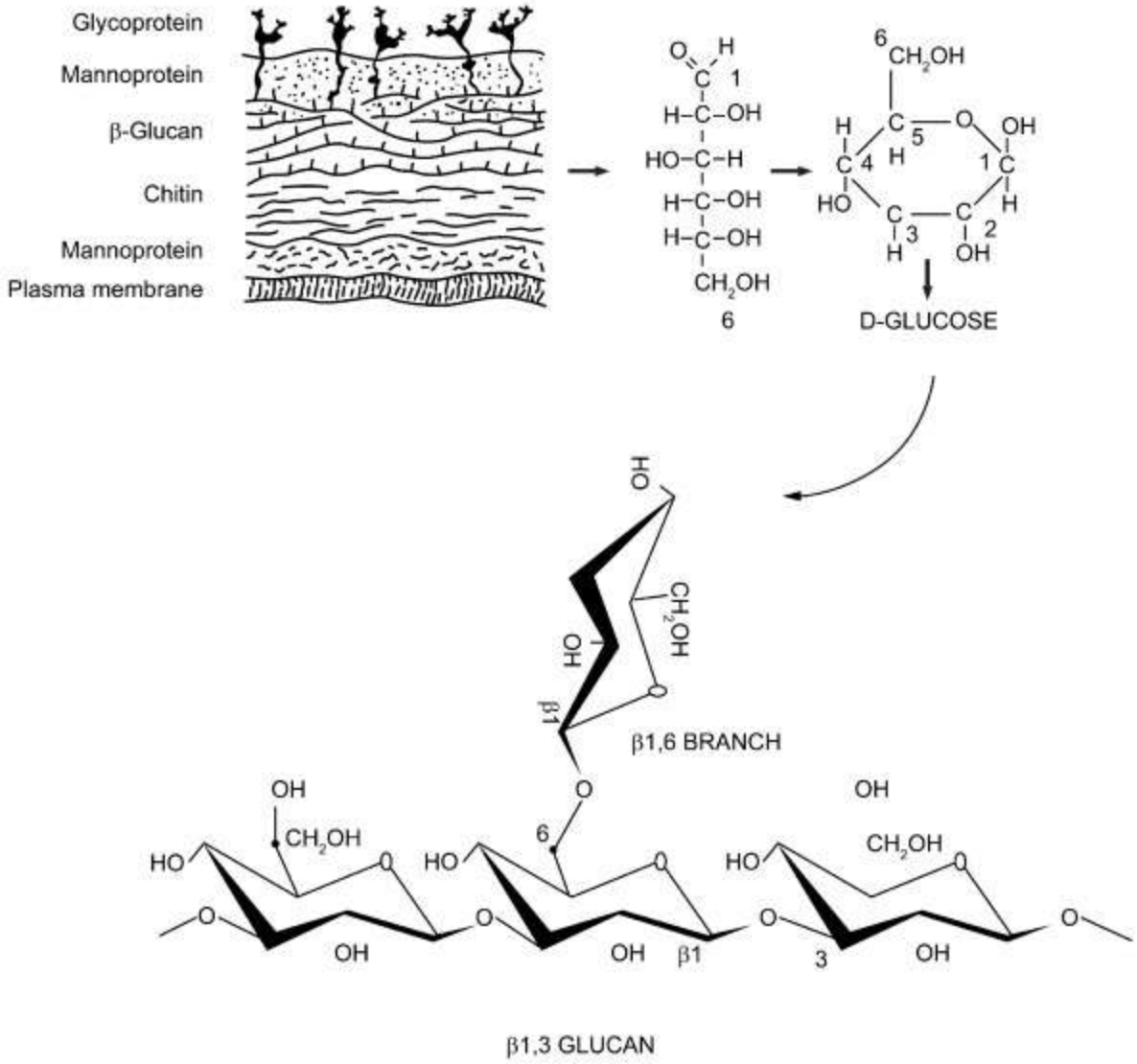
Healthcare providers sometimes give beta glucans by a shot under the skin (subcutaneously) for treating and reducing the size of skin tumors resulting from cancer that has spread.

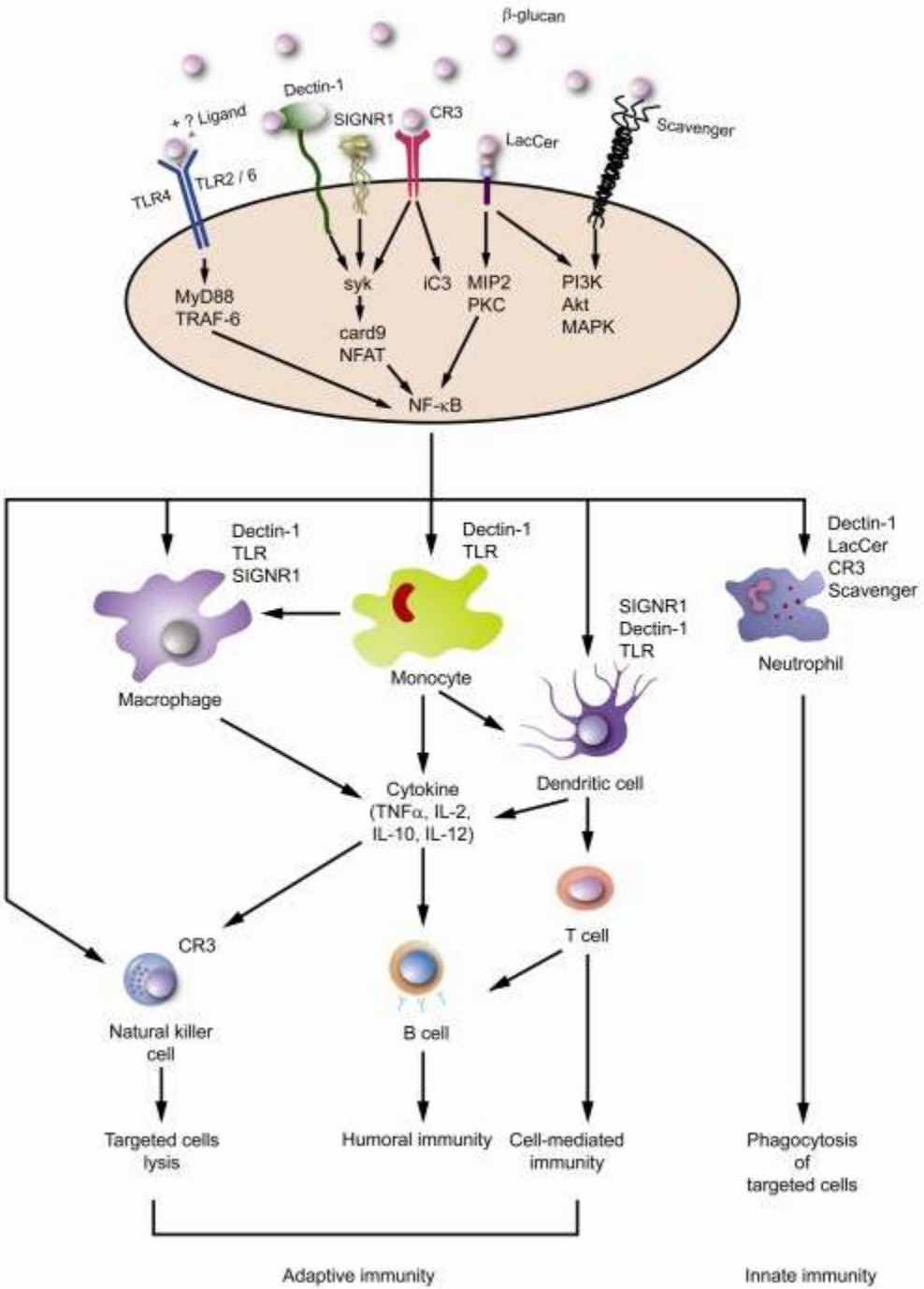
In manufacturing, beta glucans are used as a food additive in products such as salad dressings, frozen desserts, sour cream, and cheese spreads.

There are several beta glucan supplement products that claim beta glucans taken by mouth can only be absorbed if the product is prepared by a special patented process that “micronizes” beta glucan particles to a size of 1 micron or less. However, there is no reliable evidence to support such a claim.

These substances increase host immune defense by activating complement system, enhancing macrophages and natural killer cell function. The induction of cellular responses by mushroom and other beta-glucans is likely to involve their specific interaction with several cell surface receptors, as complement receptor 3 (CR3; CD11b/CD18), lactosylceramide, selected scavenger receptors, and dectin-1 (betaGR). beta-Glucans also show anticarcinogenic activity. They can prevent oncogenesis due to the protective effect against potent genotoxic carcinogens. As immunostimulating agent, which acts through the activation of macrophages and NK cell cytotoxicity, beta-glucan can inhibit tumor growth in promotion stage too. Anti-angiogenesis can be one of the pathways through which beta-glucans can reduce tumor proliferation, prevent tumor metastasis. beta-Glucan as adjuvant to cancer chemotherapy and radiotherapy demonstrated the positive role in the restoration of hematopiesis following by bone marrow injury. Immunotherapy using monoclonal antibodies is a novel strategy of cancer treatment. These antibodies activate complement system and opsonize tumor cells with iC3b fragment. In contrast to microorganisms, tumor cells, as well as other host cells, lack beta-glucan as a surface component and cannot trigger complement receptor 3-dependent cellular cytotoxicity and initiate tumor-killing activity. This mechanism could be induced in the presence of beta-glucans.

several immune receptors including Dectin-1, complement receptor (CR3) and TLR-2/6 and trigger a group of immune cells including macrophages, neutrophils, monocytes, natural killer cells and dendritic cells.


Glycoprotein
Mannoprotein
β-Glucan
Chitin
Mannoprotein
Plasma membrane
6
D-GLUCOSE
β1,6 BRANCH
β1,3 GLUCAN


β-glucan
Dectin-1
SIGNR1
CR3
LacCer
Scavenger
+ ? Ligand
TLR4
TLR2 / 6
MyD88
TRAF-6
syk
card9
NFAT
iC3
MIP2
PKC
PI3K
Akt
MAPK
NF-κB
Dectin-1
TLR
SIGNR1
Macrophage
Dectin-1
TLR
Monocyte
SIGNR1
Dectin-1
TLR
Dendritic cell
Dectin-1
LacCer
CR3
Scavenger
Neutrophil
Cytokine
(TNFα, IL-2,
IL-10, IL-12)
CR3
Natural killer
cell
B cell
T cell
Targeted cells
lysis
Humoral immunity
Cell-mediated
immunity
Phagocytosis
of
targeted cells
Adaptive immunity
Innate immunity

improve skin issues, such as acne, eczema and psoriasis. It reduces the signs of aging by reducing the appearance of wrinkles and boosting collagen production. The high concentration of the rare Omega 7 and Vitamin A intensely moisturize and encourage cell turnover for bright, clear, healthy skin and improved wound healing.

Sea buckthorn Hippophae r tory of use in folk medicine, dating back thousands of years. Tib Tang dynasty used it to help relieve various health problems. It i medicine as far back as 5000 BC.11 In 12 BC, the ancient rious health issues. In Tibet, Russia, Mongolia, and China, sea bu relieve cough, promote blood circulation, aid digestion, an

Sea buckthorn oil is well-kn and rejuvenating effects on the skin. When used topically, it's a great natural cleanser and exfoliator. It can also help heal burns, cuts, wounds, sunburn, rashes, and other types of skin damage

It contains over 190 nutrients and phytonutrients, including vitamin C, which is 12 times higher than that of an orange.13 It also contains high amounts of vitamins, minerals, fiber, and protein, making it a powerful superfood.

This berry also has as much vitamin E as wheat germ, three times more vitamin A than carrots, and four times more superoxide dismutase (SOD), an important enzyme that helps prevent free radical damage, than ginseng.14 Plus, it's the only plant source that contains omega 3, 6, 9, and 7.

Rakytníkový olej

Sea buckthorn (Hipopphae rhamnoides L.) is a plant native to Europe and Asia, but nowadays widely grown all over the world. Mostly it is appreciated for its valuable berries, although all parts are reported to be rich in a wide range of biologically active substances (Michel et al., 2012). Due to the antiviral, antibacterial, anti-inflammatory, antitumor and antioxidant properties of sea buckthorn leaves (SBL) the number of studies investigating their potential utilization has grown in recent years (Kim e adhyay et al., 2010). In mo group of hydrophilic a gated. However, th of lipophilic antioxidants anol-8 (PC-8), but also carc racts.

Petra S. Larr

Effects of se sal women: A randomize ume 79, Issue 3, Nov

Paweł Górnaś, Elga Šnē, Aleksander Siger, Dalija Segliņa
Sea buckthorn (Hippophae rhamnoides L.) leaves as valuable source of lipophilic antioxidants: The effect of harvest time, sex, drying and extraction methods
Industrial Crops and Products, Volume 60, September 2014, Pages 1–7

Isorhamnetin (Iso), a novel and essential monomer derived from total flavones of Hippophae rhamnoides that has long been used as a traditional Chinese medicine for angina pectoris and acute myocardial infarction, has also shown a spectrum of antitumor activity. However, little is known about the mechanisms of action Iso on cancer cells.

Li Q, Ren FQ, Yang CL, Zhou LM, Liu YY, Xiao J, Zhu L, Wang ZG.
Anti-proliferation effects of isorhamnetin on lung cancer cells in vitro and in vivo. Asian Pac J Cancer Prev. 2015;16(7):3035-42

long-term consumption of raw cruciferous vegetables can reduce the risk of cancer (Herr and Buchler, 2010, Higdon et al., 2007 and Keck and Finley, 2004). Chinese cabbage contains several agents commonly found in cruciferous plants, including oltipraz, phenethyl isothiocyanate, chlorophyllin, and dithiolethiones, which have also demonstrated inhibitory effects on hepatocellular carcinoma (HCC) (Mehta et al., 1994 and Suzuki et al., 2013).

Tuoyi Wang, Chunyan Li, Yang Liu, Tiezhu Li, Jie Zhang, Yonghai Sun
Inhibition effects of Chinese cabbage powder on aflatoxin B1-induced liver cancerFood Chemistry, Volume 186, 1 November 2015, Pages 13–19