

Cancer and nutrition: Molecular mechanisms

VG
NETT

Helse

Ily venner? Her finner du mange som søker mye kontaktil.

Søk i VG Nett | Søk | Søk på Internett | Søk

Bli fadder nå

Redd Barna

Jeg vil gi

Selha skolegang
 barna mine større julegaver

Diskuter Helse

Kvinne som har passert overgangsalderen, kan redusere risikoen for å utvikle kreft med hele 35 prosent ved å ha en sunt livsstil.

Det viser en ny amerikansk undersøkelse publisert i fagtidsskriftet Cancer Epidemiology, Biomarkers and Prevention.

Tekst en venn - Mest pop @ Facebook.com/verdenshelse og @Verdenshelse

Understolen så på løssten til 29564 kvinner i alderen 55-69 år over en periode på 15 år. Alle hadde passert overgangsalderen.

SPIS FRUKT: Studiet viser at det spesielt er artikelskjæret i frukt og grønnsaker som beskytter mot blant annet kreft. Foto: SØLRUN THØMSEN

Sunn stil minsker kreftfare

Kvinne som har passert overgangsalderen, kan redusere risikoen for å utvikle kreft med hele 35 prosent ved å ha en sunt livsstil.

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BARNAS Juletilbud hos

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Helse

På Jahr etter nye vinner? Be soñ Motoplassen! Søk i VG Nett | Søk | Søk på Internett | Søk

Kids fashion

www.kidsfashion.no

Tid til overs? 100vis av nettsider å velge mellom

Diskuter Helse

Frøtt mangel som er under 1541 kalorier? Piller jeg Skjærtell (31 innlegg)?

Tekst en venn - Mest pop @Facebook.com/verdenshelse og @Verdenshelse

Kids fashion

Polser og kjøttmat gir økt kreftfare

For dem som er gladi polser, karbonader og annen bearbeidet rød kjøttmat har forskere en ubehagelig oven avslørte.

©OLIO, MCN, FARGO: Spiser du mye polser, kan det ikke foran for kreft i kroppen din. Foto: Silje Løberg Sulum

OGILIO, MCN, FARGO: Spiser du mye polser, kan det ikke foran for kreft i kroppen din. Foto: Silje Løberg Sulum

Mattarene kan gi deg kreft - i tillegg til kreftfarene ved at de inneholder mye salt og kolstørstok.

VG Nett følger:
Helse og medisin
Mat

Finn oppdaterer i Motoplassen

BARNAS Juletilbud hos

VG Nett 6. april 2010

Ytterhundrekkant i sykehuset:
Dil kretsykeler medt i Oslo.
Heldt eller dødt?

Dårlig ånde - borte på 3 min.
Ca 70% av alle voksne personer
kan ha problemer med dårlig ånde

Gjettarberet!

Prøv en helt ny berøringspleievele
gratiss!

Økt sekretat!
Leget for mosen og virker godt.

Mageproblemene er portet:
For mye brukere har fått hjel.
Prøv Lection-Mage gratis 2 min.

Vælg kategori

Armonis informasjon

VG QuickBanner:
Bli nyresykepleier midt i Oslo!

DIAKONOVIA
Helsekontor Drontheim

Øk dine vinner-

- Mat påvirker neppe kreftrisiko

Av Steinar Quenius Andersen 06.04.2010 kl. 07:50 Kilde: VG

Professor Vinjar Fonnebo mener vi tillegger maten allfor stor betydning for utvikling av kreft.

SVARTER DEDATT: Professor Vinjar Fonnebo mener vi tillegger maten allfor stor betydning for utvikling av kreft. Foto: Øystein Rønning

Fonnebo, som er direktør ved Nasjonal forskningsstasjon for komplementær og alternativ medisin (NAFKAM) i Trondheim, forsør av han stårker hånden inn i et vepsbol.

Helse og medisin

22-åring døde etter kneoperasjon - sykehus straffes

(VG Nett) Ringingen sylkehushus har fått en foretakstraff i form av et forslag på 500.000 kroner etter at en 22-åring døde etter en kneoperasjon.

[Les hele saken](#)

Navarsæte vil fryste nedleggelsesprosesser

Ln Signe Navarsæte (Sp) ber helseminister Anne Grete Strøm-Erichsen (Ap) øyblikkelig fryste alle prosesser i helseforetakene som tar sitt på å legge ned sykehushos.

[Les hele saken](#)

Böhler: - Helsefarlig å frede lokalsykehusene

Jan Bohler (Ap) advarer i sterke orddrag mot å frede samtlige lokalsykehus i Norge slik de fungerer i dag.

[Les hele saken](#)

Ring 22 95 75 00

Volvat
med vennlighet

Helse og medisin | **RSS**
[www.vg.no/rss](#)

HVORFOR IKKE TA ET

Aftenposten Nett 7. april 2010

Aftenposten.no Nyheter Helse

Alt innhold Nyheter Sport Meninger Økonomi Kultur Ulosopps Helsekriter Helse Mat og vin Jobb Bolig Varer

Internasjon Verden Politikk Kino Sosialrapport Falstad Vitens Konsernet Helse Lenvit Doktor 100

Grillsesongen starter hos REMA 1000

KYLINGFILET 39,-

GRILL

REMA 1000

AFTENPOSTEN EAVIS

«Fem om dagen» hjelper lite mot kreft

Frukt og grønnsaker hjelper ikke i like stor grad mot kreft som forskerne hittil har trodd.

AV ELISABETH ROOIM

Oppdatert 07.04.2010 kl. 14:39 | Publisert 07.04.2010 kl. 12:47

«Fem om dagen» tyder den igjen øppningene fra helsemyndighetene. Men en undersøkelse av 500 000 mennesker viser at frukt og grønt i medie grad følges opp av kreftsykdommen enn tidligere antatt.

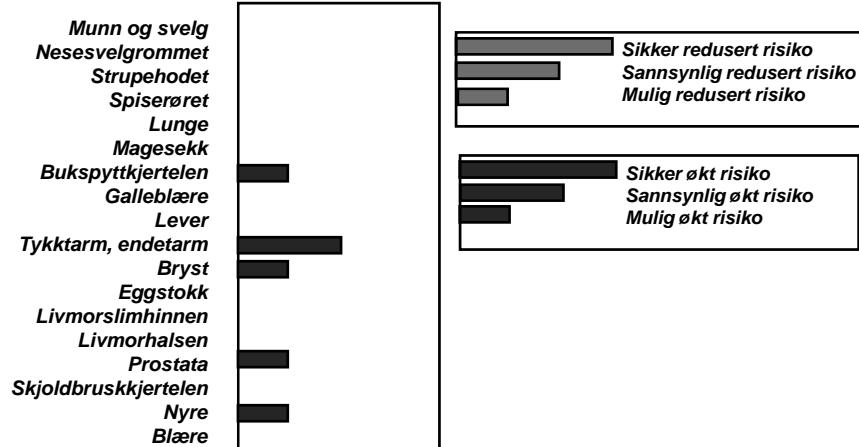
DOLMUS
EksamensMarkedet

Tips om boligskatt

Kjøp dagens eAvis

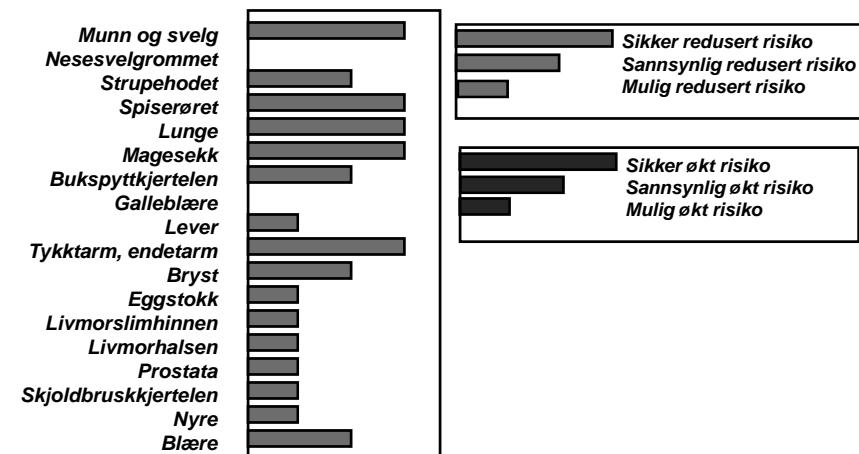
World Cancer Research Fund: Lifestyle and Cancer 1997

Rødt kjøtt



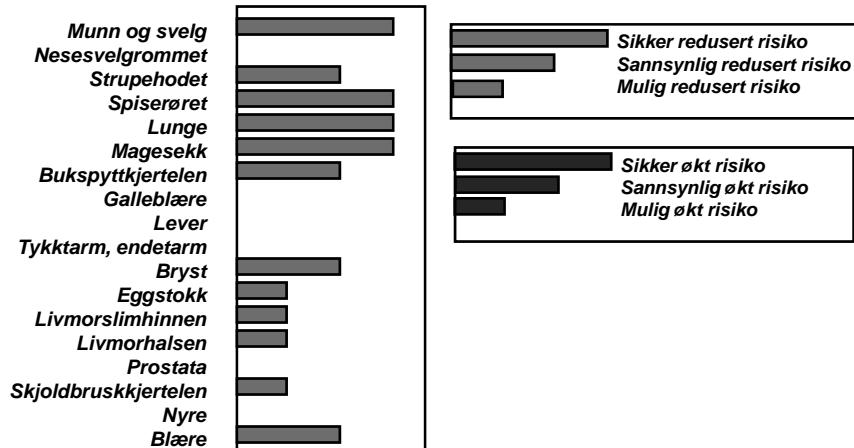
World Cancer Research Fund: Lifestyle and Cancer 1997

Grønnsaker



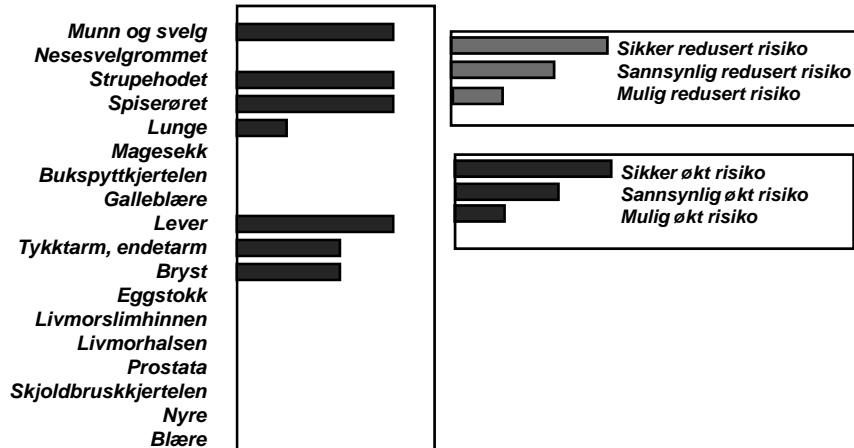
World Cancer Research Fund: Lifestyle and Cancer 1997

Frukt



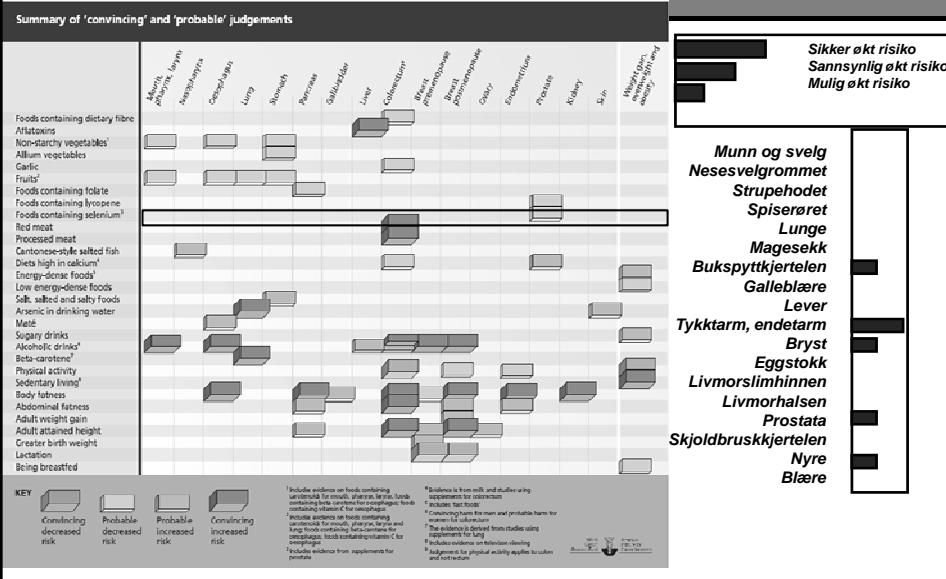
World Cancer Research Fund: Lifestyle and Cancer 1997

Alkohol



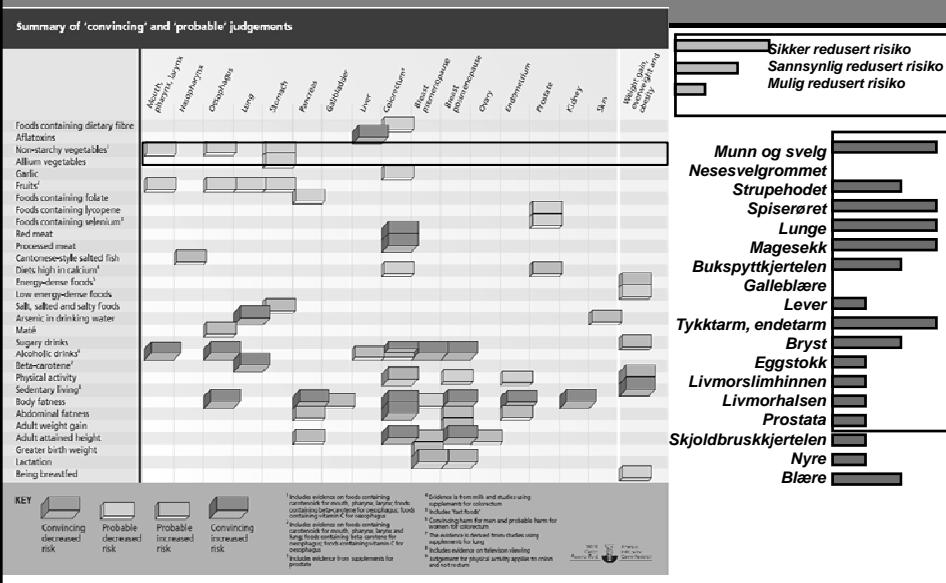
World Cancer Research Fund Lifestyle and Cancer 2007

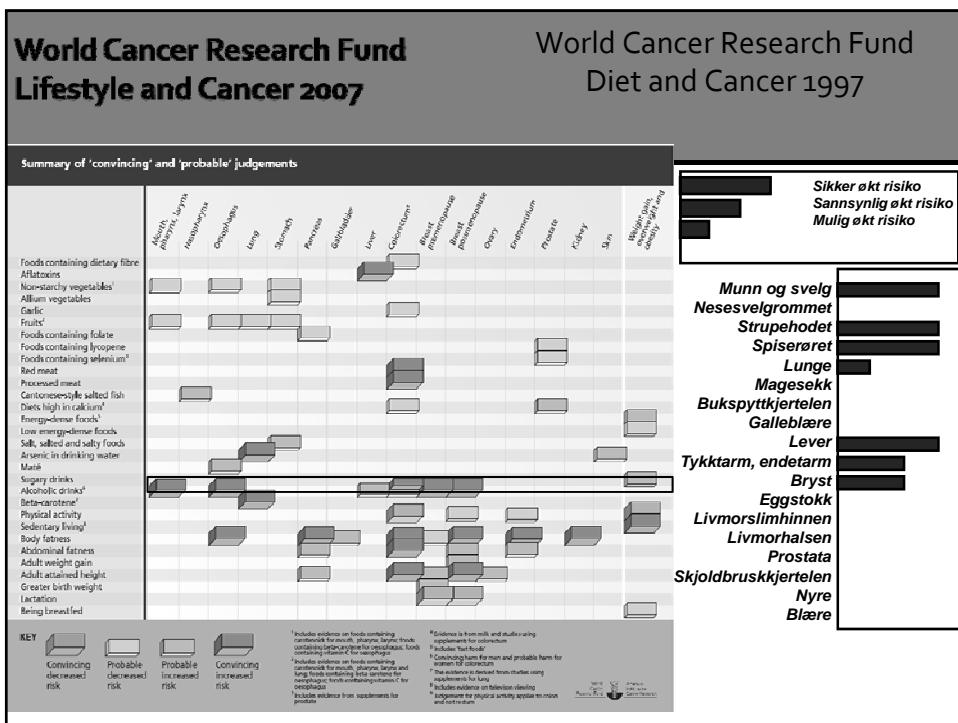
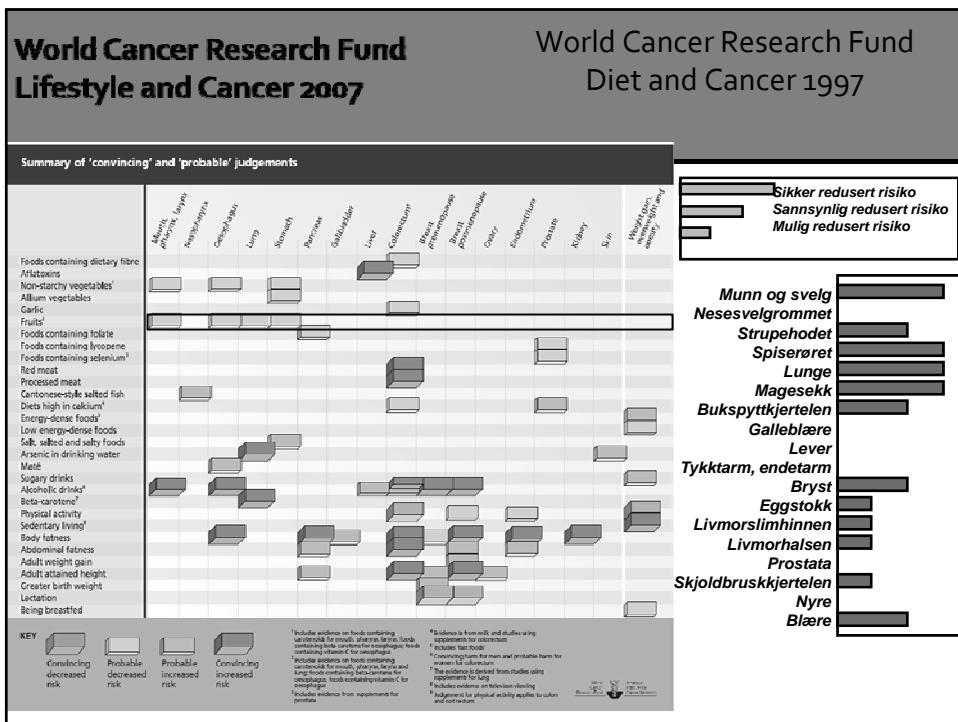
World Cancer Research Fund Diet and Cancer 1997



World Cancer Research Fund Lifestyle and Cancer 2007

World Cancer Research Fund Diet and Cancer 1997





Message:

Our knowledge about the relationship between diet and cancer risk is dynamic, and requires a constant update based on current high quality research.

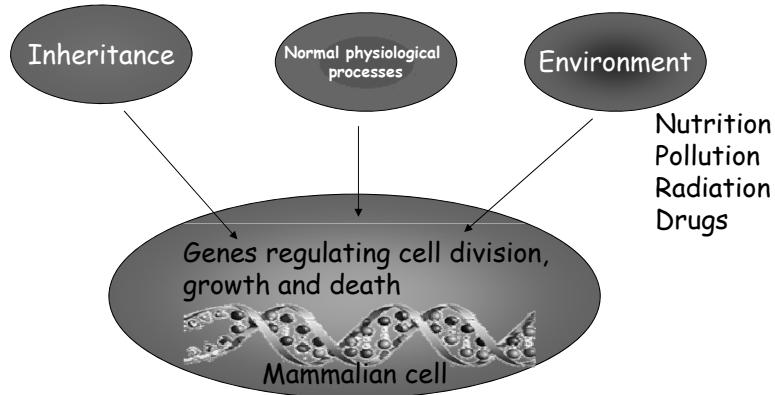
Cancer and Nutrition

- Characteristics of cancer cells
- Types of cancers
- Molecular mechanisms in cancer development
- Interactions with diet
 - Folate
 - Phytoestrogens
 - Phytochemicals/polyphenols
- Adverse effects of dietary components

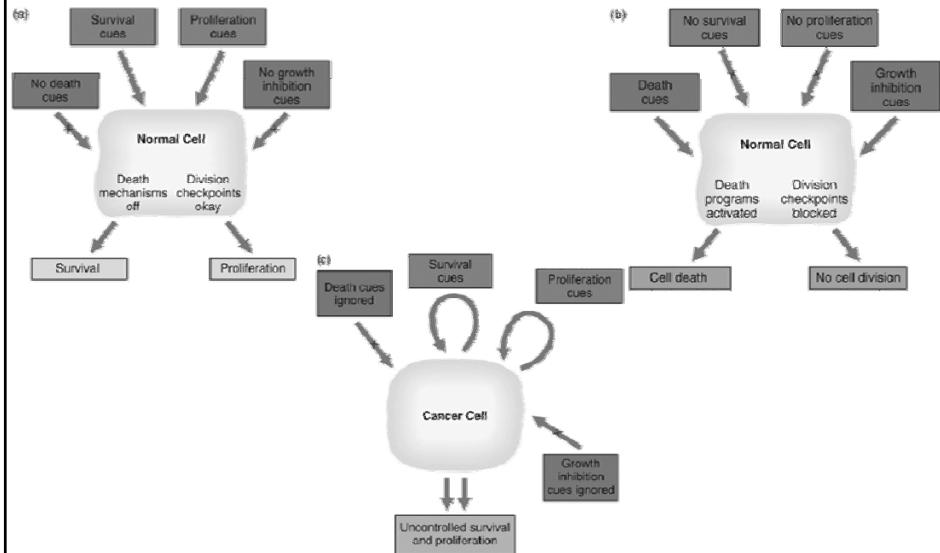
Cell-transformation – tumor development

- Cancer is a genetic disease!
- Caused by DNA damage/specific mutations
 - Deregulated cell growth
 - Immortalization
 - Invasion - metastasis
 - Angiogenesis

Factors influencing gene expression and function

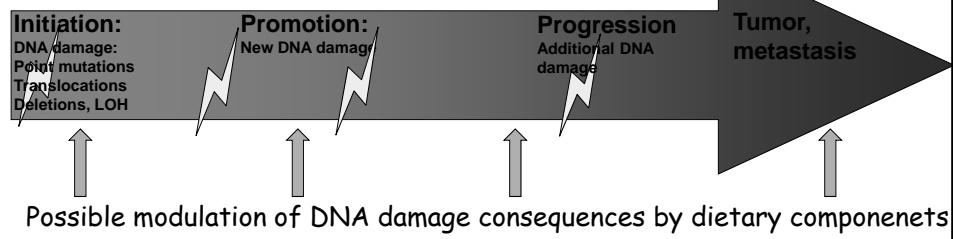


The characteristics of cancer cells

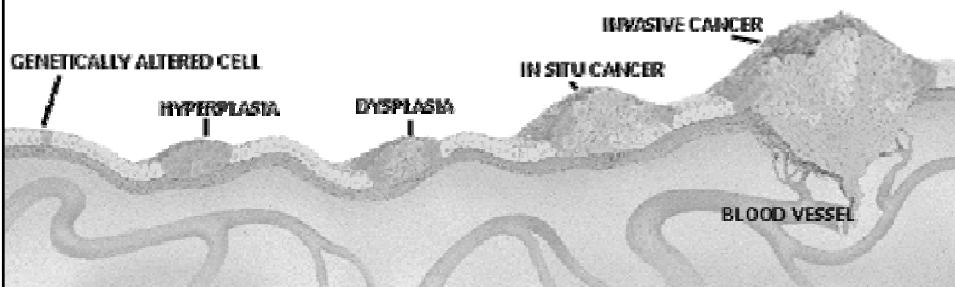


Cell-transformation – tumor development

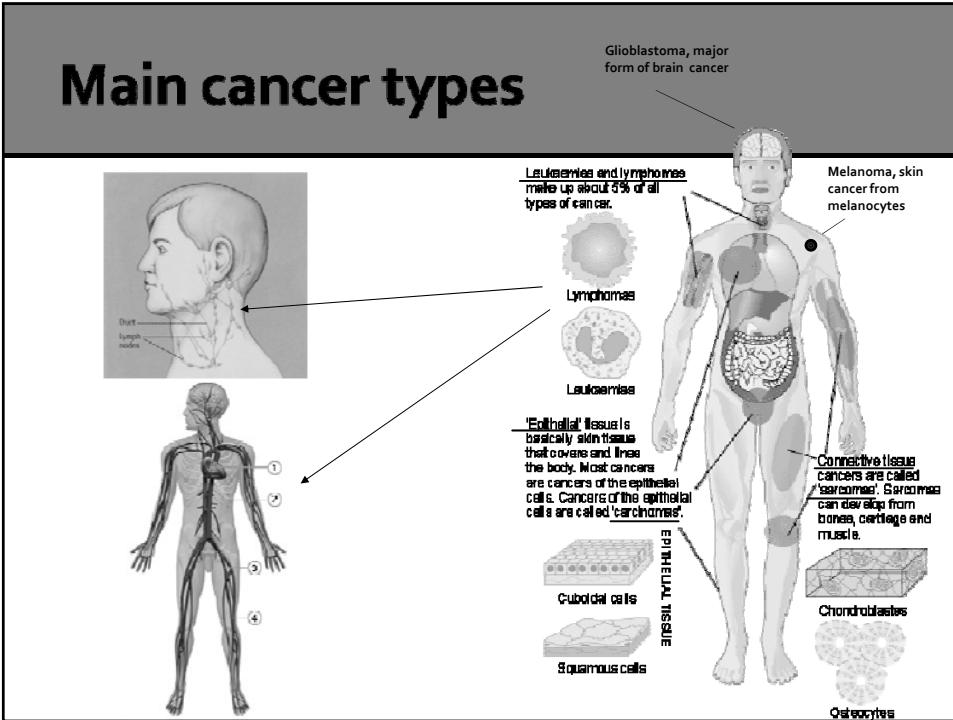
- Cancer is a genetic disease!
 - Deregulated cell growth
 - Immortalization
 - Invasion
 - Angiogenesis



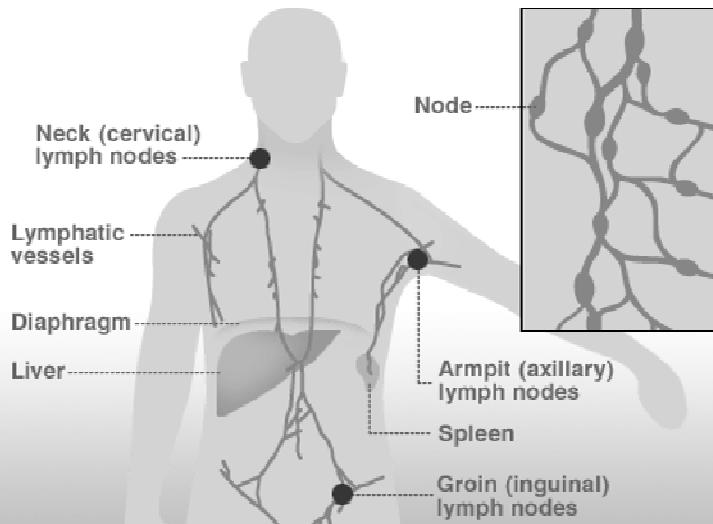
Cancer development: a multi step process



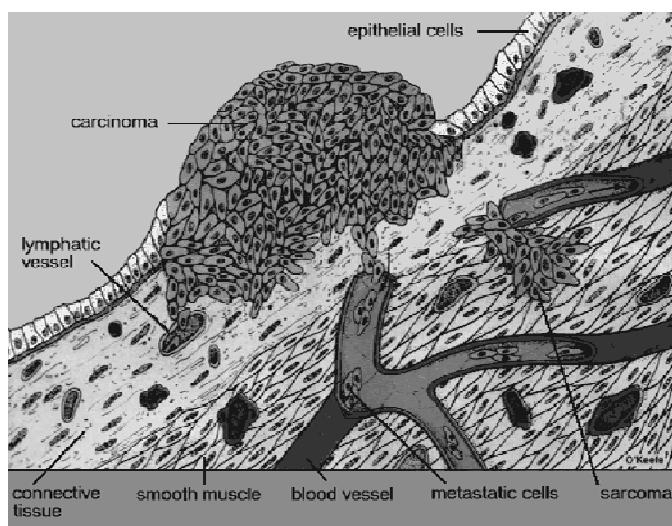
Main cancer types



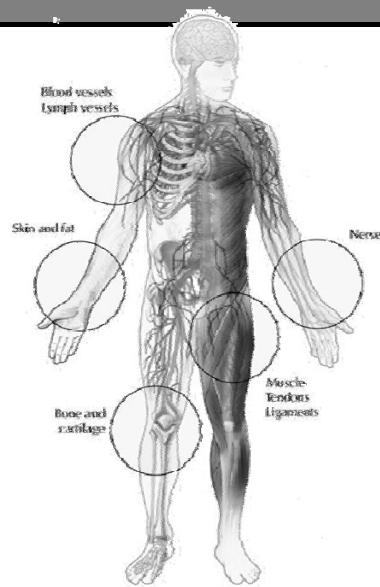
Lymphoma



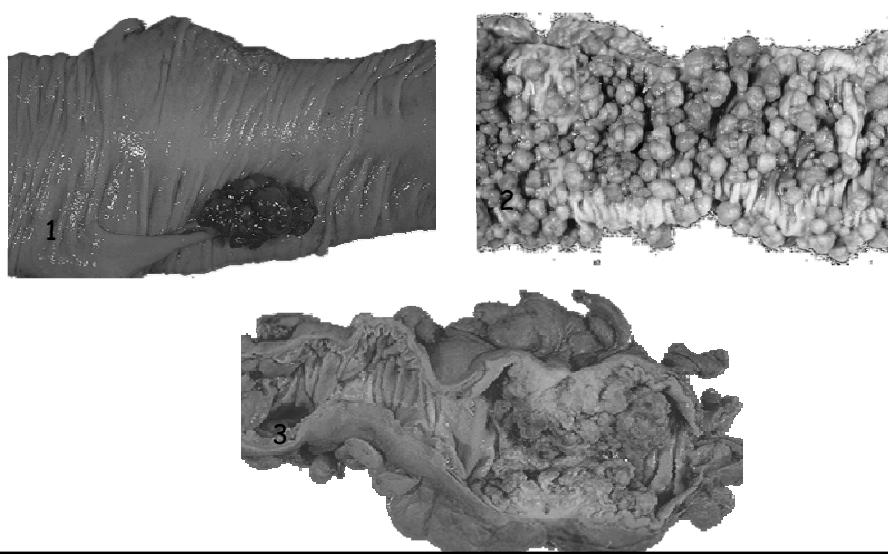
Carcinoma



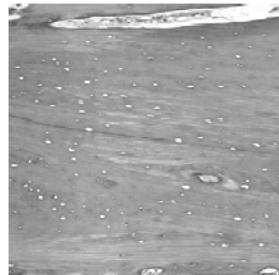
Sarcoma



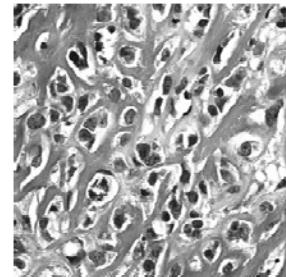
Colon cancer



Cancer in the microscope

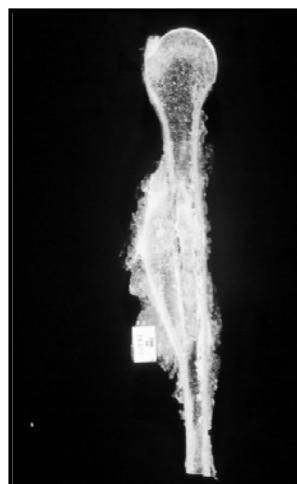


Normal bone tissue



Bone cancer (osteosarcoma)

Macroscopic bone cancer



Ewing sarcoma



Osteosarcoma in femur

Major cellular signalling pathways are altered in cancer cells

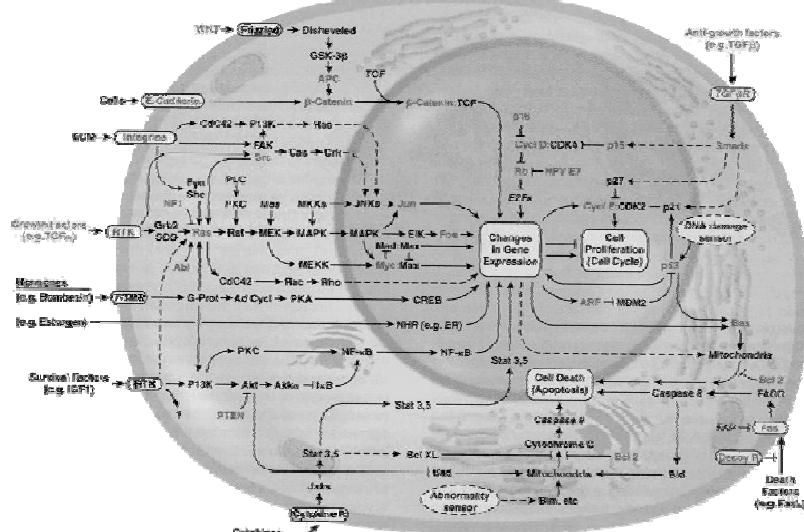


Figure from Hanahan and Weinberg, 2000, Cell 100, p. 57-70

Important genetic changes in established cancer cell lines.

Cell line	Histology and subtype ^a	Genetic and epigenetic alterations ^b										Oncogene	
		p53	RB	p14	p15	p16/ARF	FAT1	PTEN	SMAD4	TGFBR1	MYC198	PAPPA	
LU24	SOC	Mut	Mut										HD
Lu135	SOC	Mut	Mut										
NA17	SOC	Mut	Mut										Amp
NCI-H209	SOC	Mut	Mut										Mut
Lu119	SOC	Mut											HD
NCI-H468	SOC	Mut											Amp
NA14774	SOC	Mut											Mut
SPC-A	SOC	Mut	Mut										HD
NCI-H434	SOC	Mut	Mut										Amp
NCI-H59	SOC	Mut											Amp
NCI-H92	SOC	Mut											Amp
MS10	SOC												
NCI-H382	ADC	Mut		HD	HD	HD							
PC-9	ADC	Mut		HD	HD	HD							
PC-14	ADC	Mut		HD	HD	HD							
PERF-LCOK	ADC	Mut		HD	HD	HD							
VMR-CLCD	ADC	Mut		HD	HD								
MS-17	ADC	Mut		HD	HD	HD							
MS-24	ADC	Mut		HD	HD	HD							
PC-9	ADC	Mut											
MS-1	ADC	Mut											
MS-29	ADC	Mut		Mut			HD						
PERF-LOMS	ADC	Mut		Mut	HD								
ABC-1	ADC	Mut		Mut									
NCI-H73	ADC	Mut		Mut									
NCI-H811	ADC	Mut		Mut									
MS-10	ADC	Mut		Mut									
PC-27	ADC	Mut		HD	HD	HD							
MS-49	ADC	Mut		HD	HD	HD							
MS-26	ADC	Mut		Mut									
LC158	SOC	Mut		HD	HD	HD							
NCI-H447	SOC	Mut		Mut	Mut								
NCI-H520	SOC	Mut		Mut									
ES-1	SOC	Mut		Mut	HD	HD							
PC-10	SOC	Mut		Mut	HD	HD							
MS-28	LCC	Mut		Mut	HD	HD							
Lu59	LCC	Mut		Mut	HD	HD							
Lu58	LCC	Mut	Mut	Mut									
MS-3	LCC	Mut	Mut	Mut	HD	HD							
PC-13	LCC	Mut	Mut	Mut	HD	HD							
NCI-H4155	LCC	Mut	Mut	Mut	Mut	Mut							

^a LCC, small cell carcinoma; ADC, adenocarcinoma; SOC, squamous cell carcinoma; SNC, adenosquamous carcinoma; LCC, large cell carcinoma.
^b Mut, mutation; HD, hemizygous deletion; Met, hypermethylation; —, loss of expression (either for p53 only); Amp, amplification; blue, inactivation of tumor suppressor gene; pink, activation of oncogene; gray, not examined; black, no alteration.

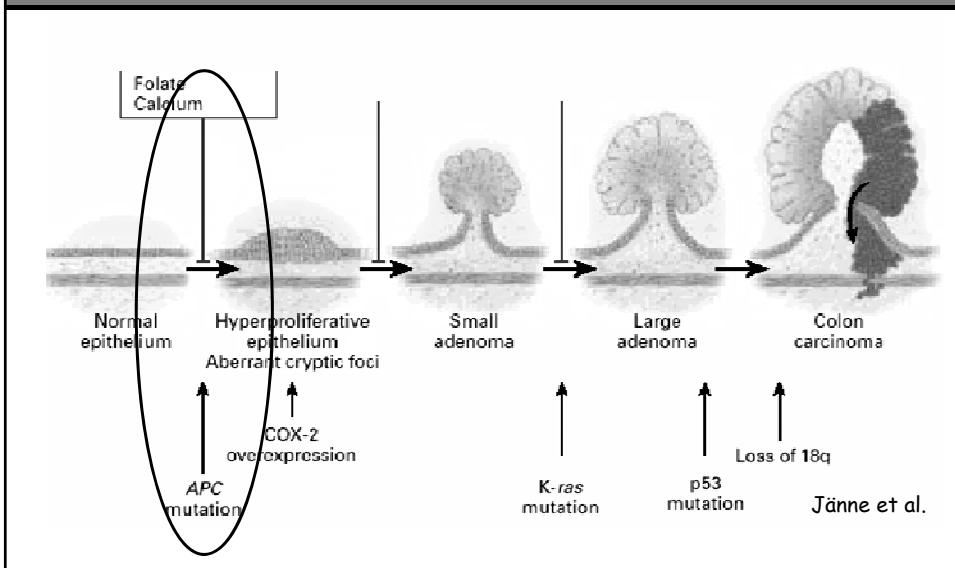
Principles for interactions between dietary factors and cancer related processes.

- Influence of dietary factors on:
 - Protein kinase modulators in cell signaling
 - DNA stability, mutation rate
 - Detoxification of carcinogens
 - Ligands for transcription factors

Cancer: Molecular mechanisms

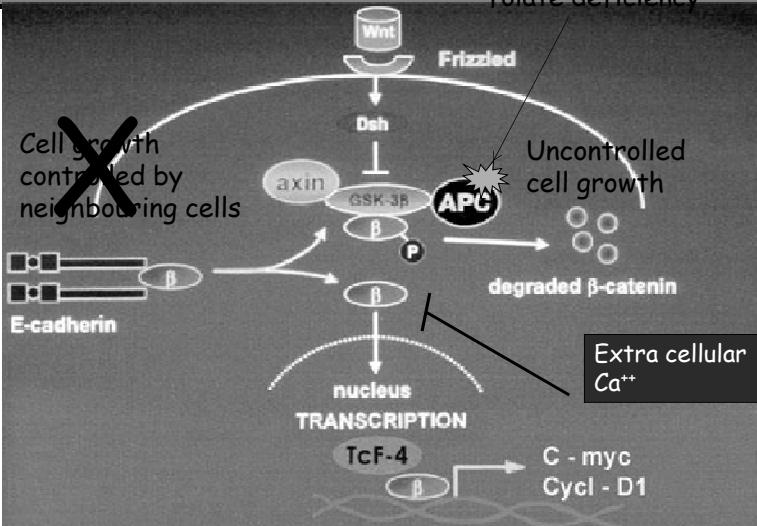
- Examples of how nutrition may interact with basic factors in cell proliferation and growth such as oncogenes and tumor suppressor genes: colon cancer and breast cancer
 - APC: Protein involved in cell proliferation
 - P53: Transcription factor involved in stress management
 - K-ras: GTP-binding protein signalling effects of growth factors
 - PTEN: Phosphatase involved in signalling of cell growth

Cancer development: a multi step process: Molecular events in colon cancer

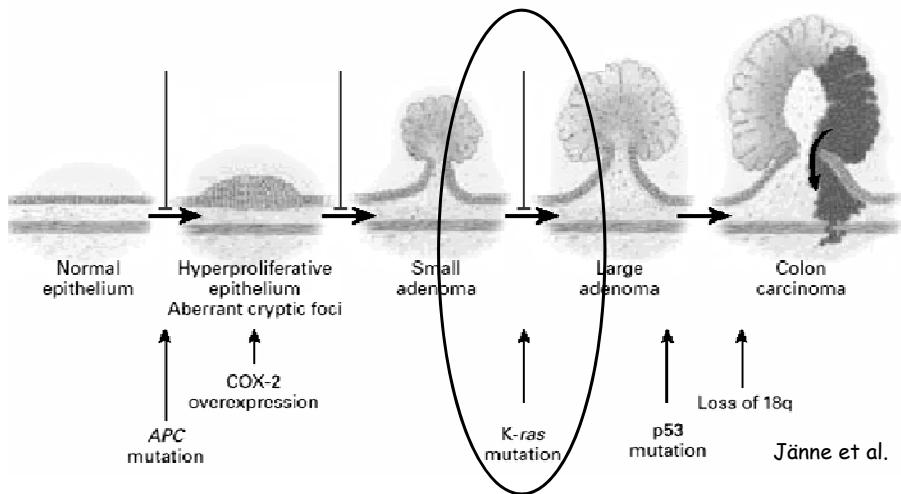


APC and nutrition

Increased mutagenesis in folate deficiency



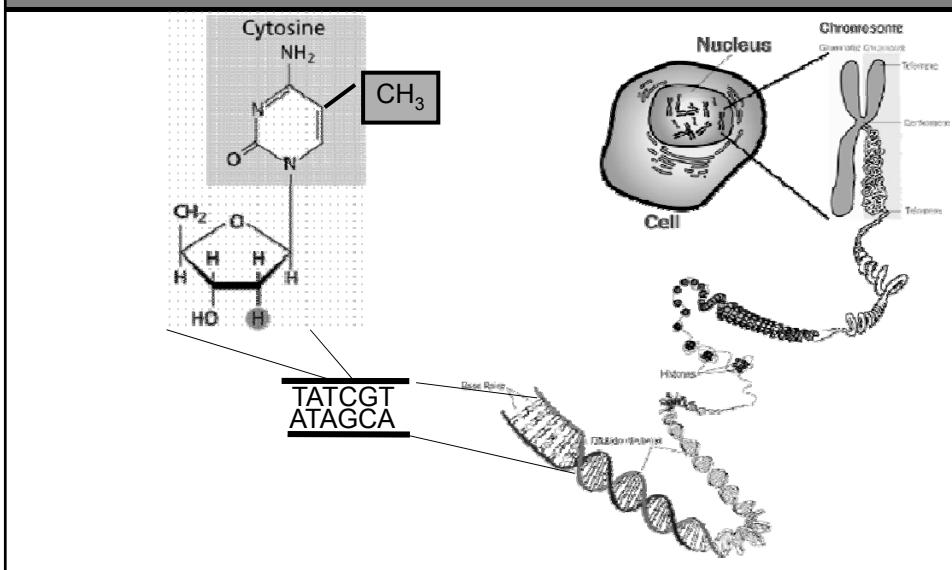
Cancer development: a multi step process: Molecular events in colon cancer



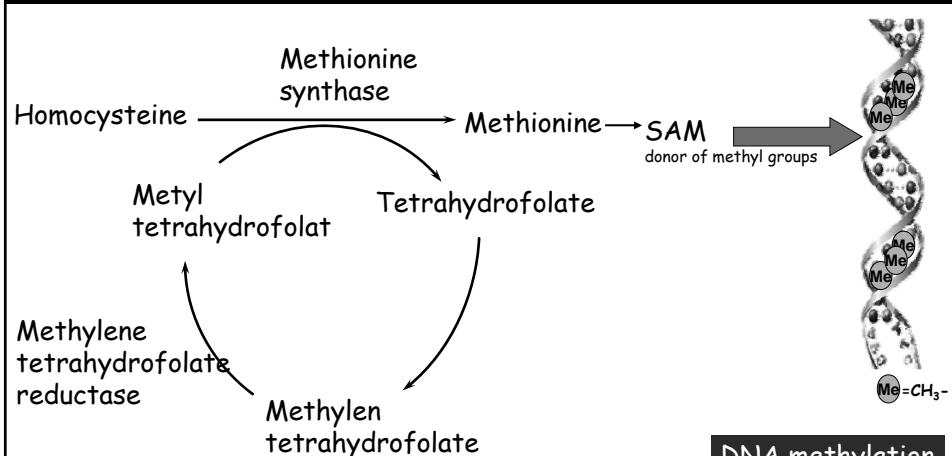
DNA methylation

- Epigenetically regulate gene expression:
 - X-chromosome in females.
 - Growth regulating genes:
 - Oncogenes (c-myc, Ki-ras)
 - Tumor suppressor genes
 - Transposons, jumping genes

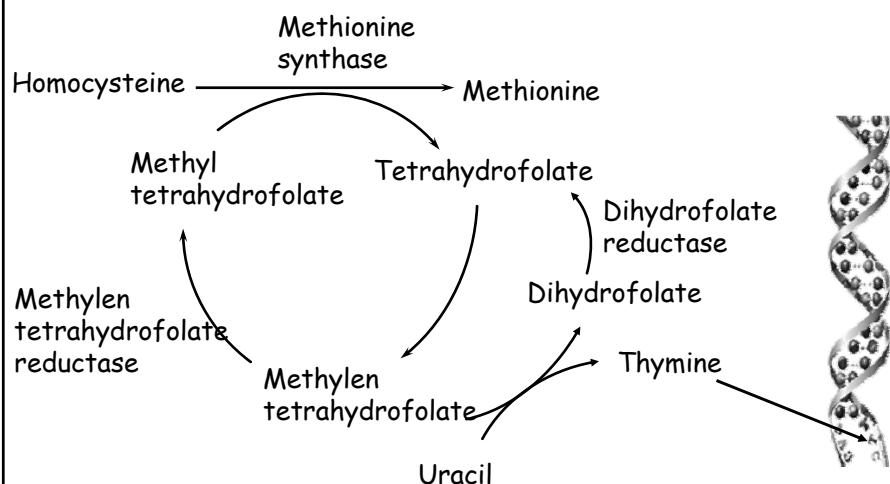
DNA methylation



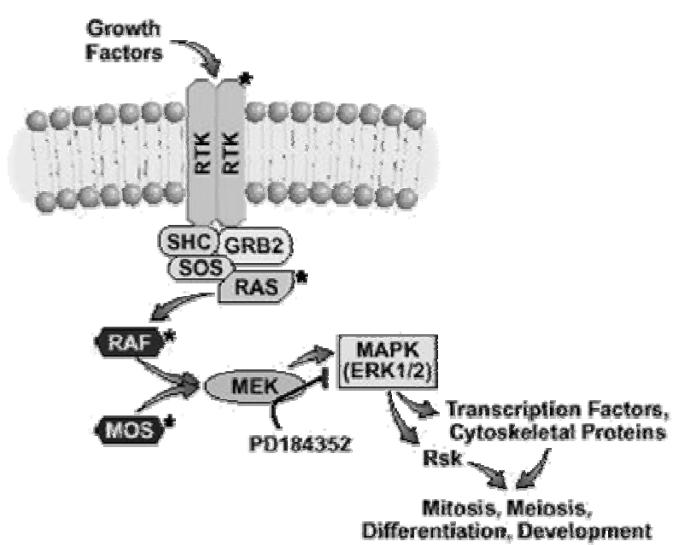
Biochemical role of folate



Role of folate in DNA synthesis



Function of Ras



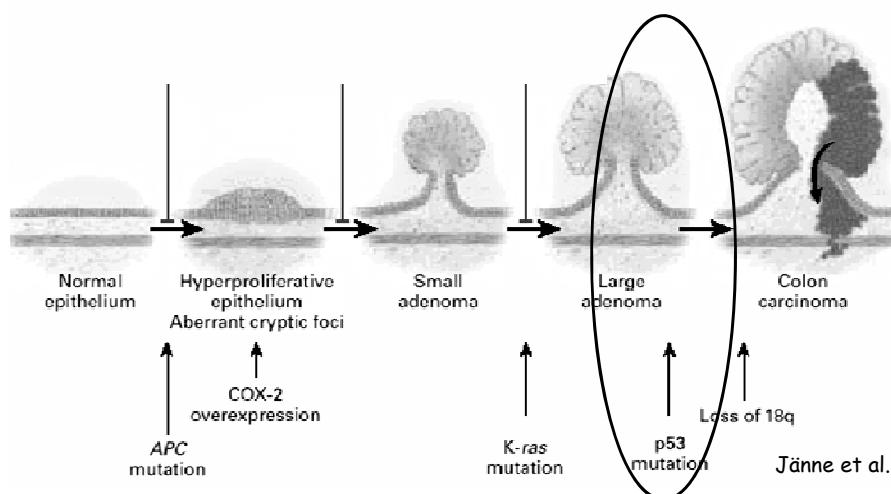
K-ras and nutrition

- Analyses of colorectal carcinomas in humans suggest association between K-Ras mutation and folate intake.

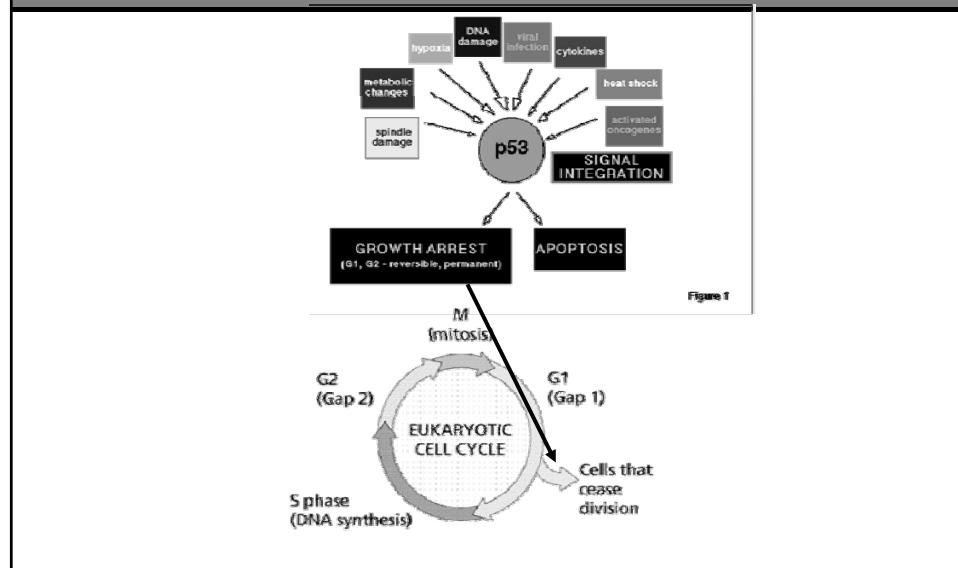
van Engeland M, et al. Effects of dietary folate and alcohol intake on promoter methylation in sporadic colorectal cancer: the Netherlands cohort study on diet and cancer. *Cancer Res.* 2003 Jun 15;63(12):3133-7.

Brink M, et al. Dietary folate intake and k-ras mutations in sporadic colon and rectal cancer in The Netherlands Cohort Study. *Int J Cancer.* 2005 May 1;114(5):824-30.

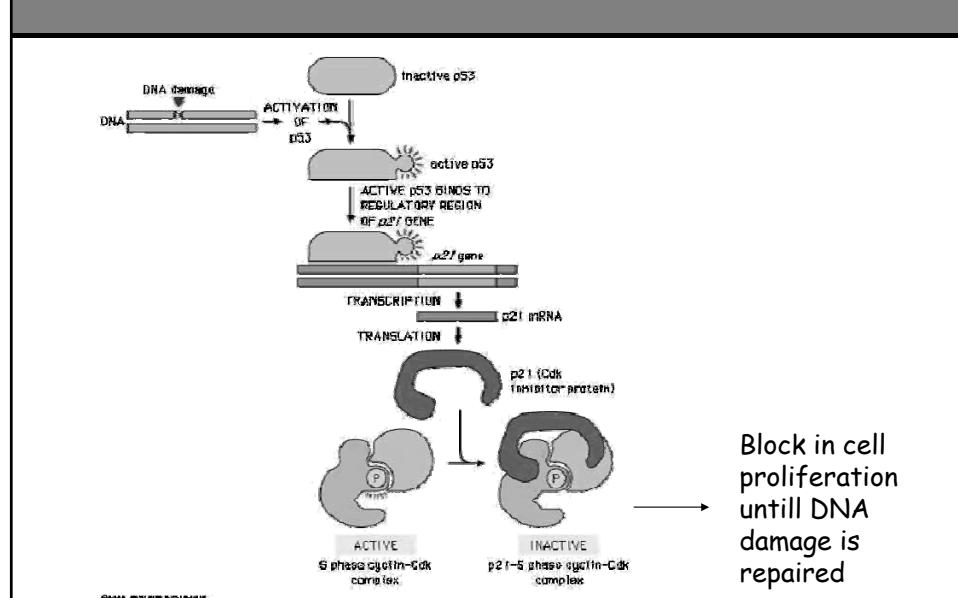
Cancer development: a multi step process: Molecular events in colon cancer



Function of p53 tumor suppressor

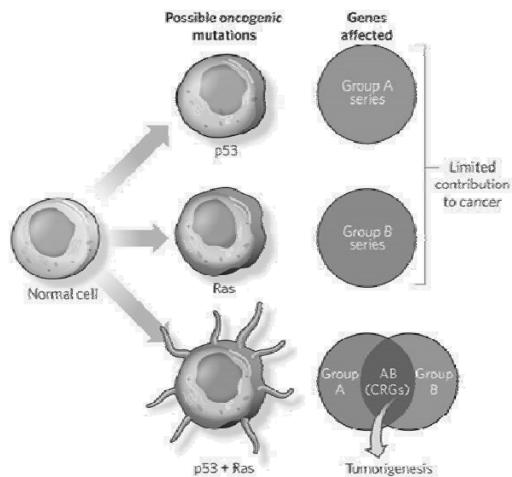


Function of p53

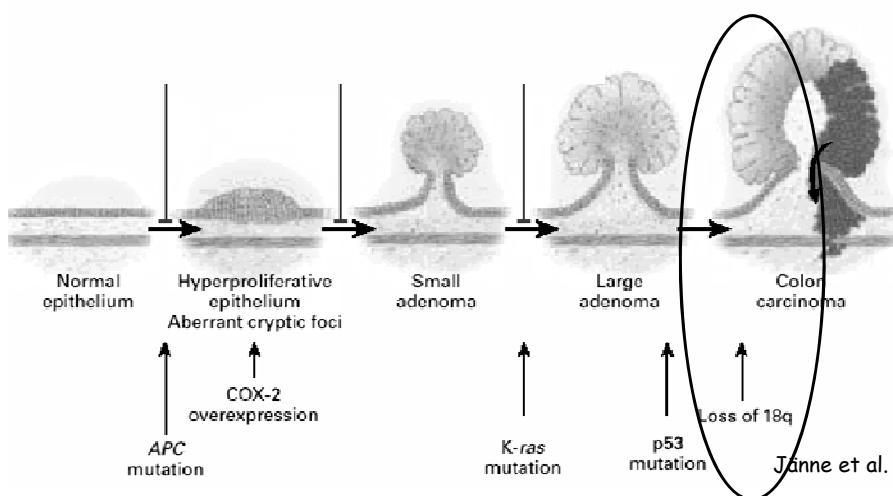


P53 and nutrition

- Folate deficiency cause DNA hypomethylation and increased risk of subsequent mutations in p53.

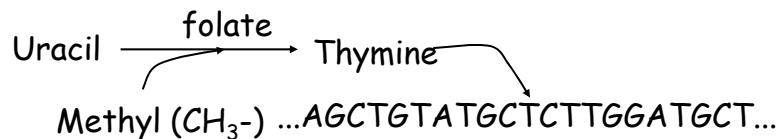


Cancer development: a multi step process: Molecular events in colon cancer



Role of folate in DNA synthesis

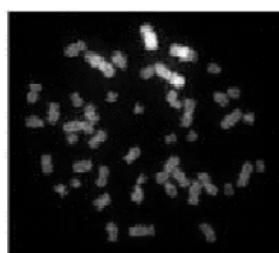
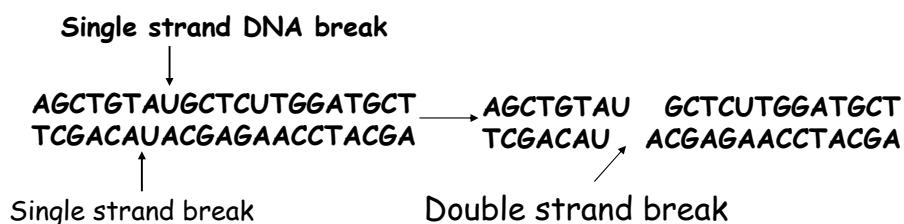
Sufficient folate:



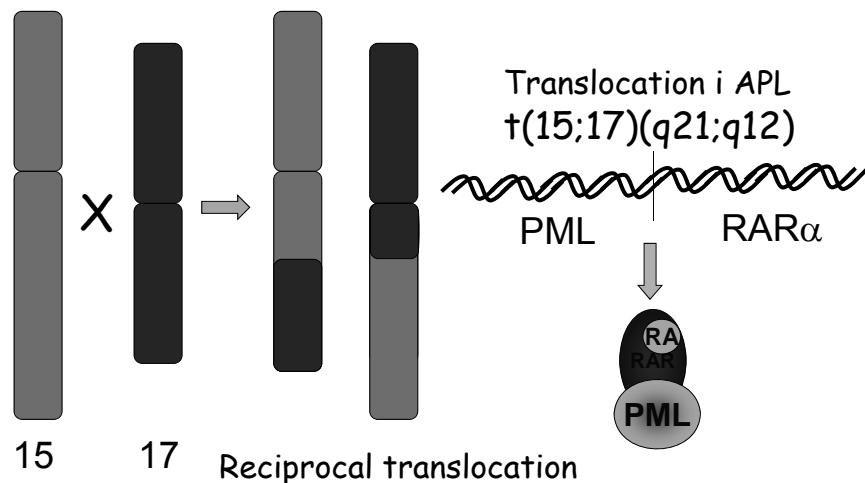
Folate-deficiency:



DNA breaks and translocation

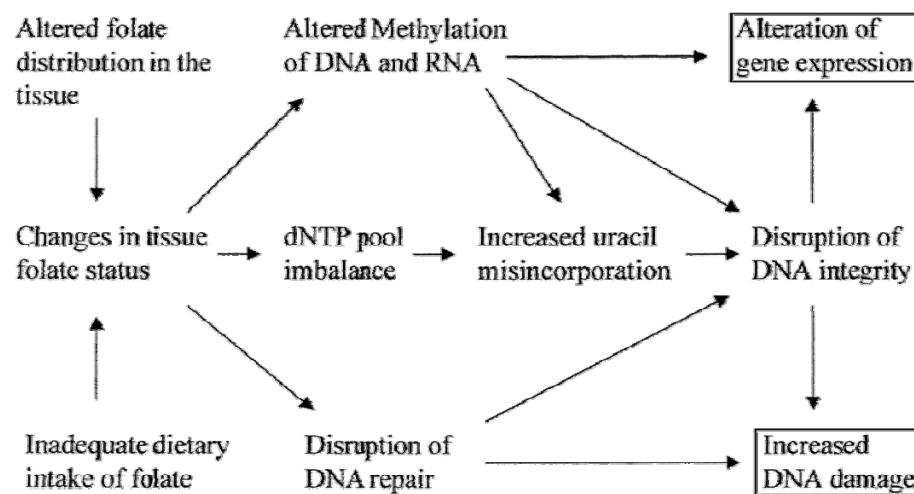


Chromosome translocation in acute promyelocytic leukemia



Message:

Changes in folate metabolism may influence several processes in cancer development



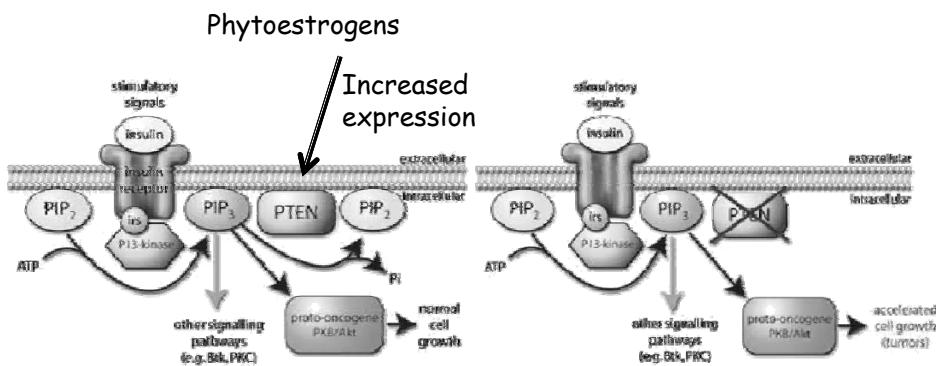
Breast cancer and the tumor suppressor PTEN



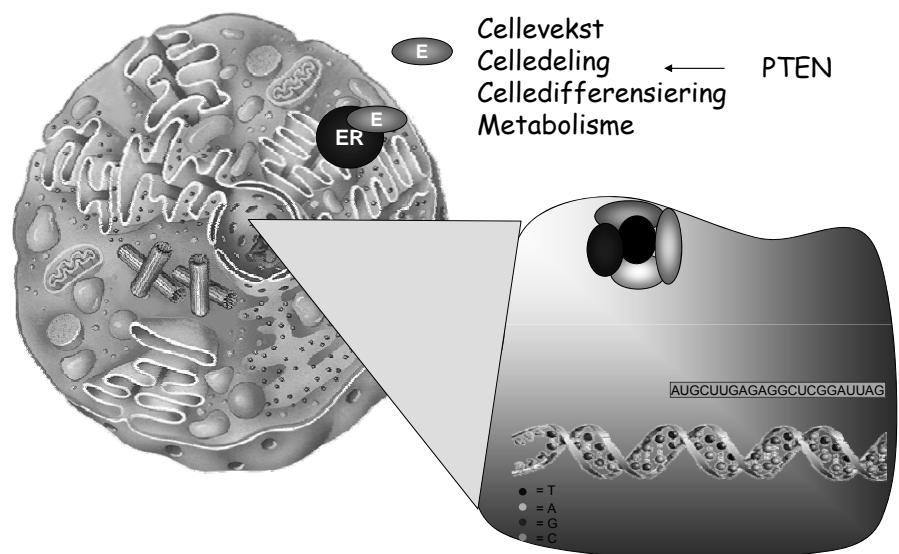
Epidemiological data suggest that diets rich in phytoestrogens protect against breast cancer.

Phytoestrogens are dietary plant components with estrogen/antiestrogen activities

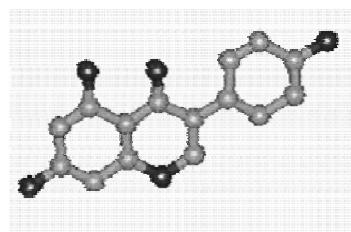
Function of PTEN



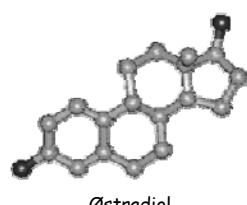
Estrogen in gene regulation



Phytoestrogens:
Plant substances with structures similar to estrogen



Genistein:
Weak estrogen-effect,
competes with estrogen for
binding to estrogen receptor



Tyrosine kinase inhibitor: 2,5 -
40 μ M
Oncogenes src, fes og abl
inhibited by 10-100 μ M genistein

Soy-rich diet \Rightarrow 5-10 μ M genistein
in the blood after 8 hours

Message:

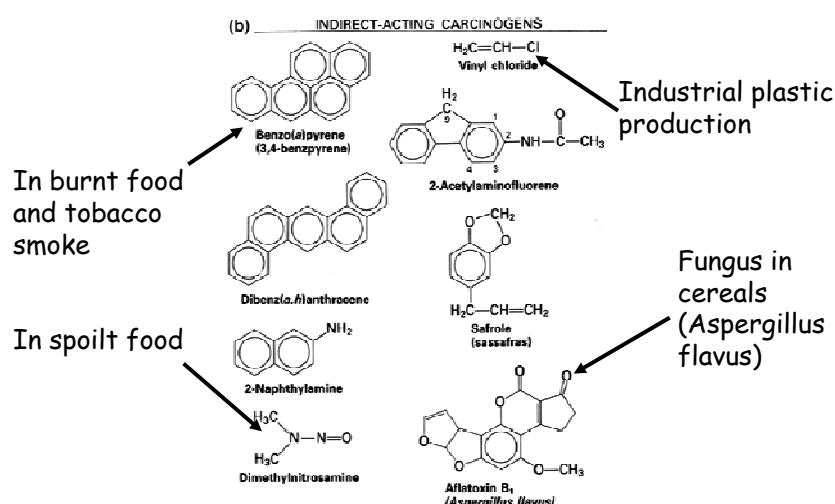
The effect of phytoestrogens (weak estrogens) are difficult to assess, since estrogen competition may be positive:

In increasing PTEN expression in estrogen negative cells

but negative:

In reducing PTEN expression in estrogen positive cells
(due to the weaker estrogen activity than estrogen itself)

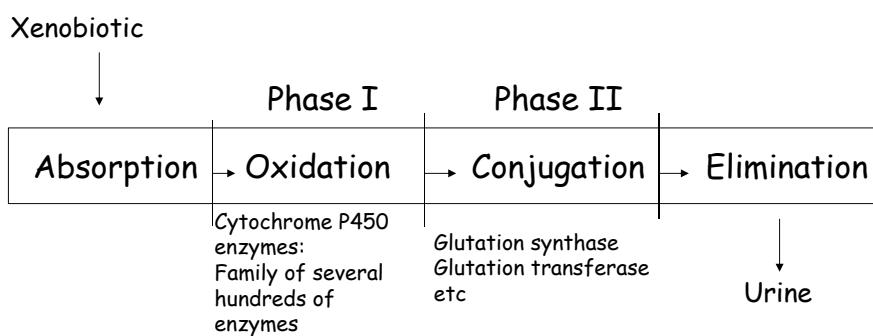
Typical procarcinogens: Requires activation to become carcinogens



Plant substances are de facto xenobiotic substances

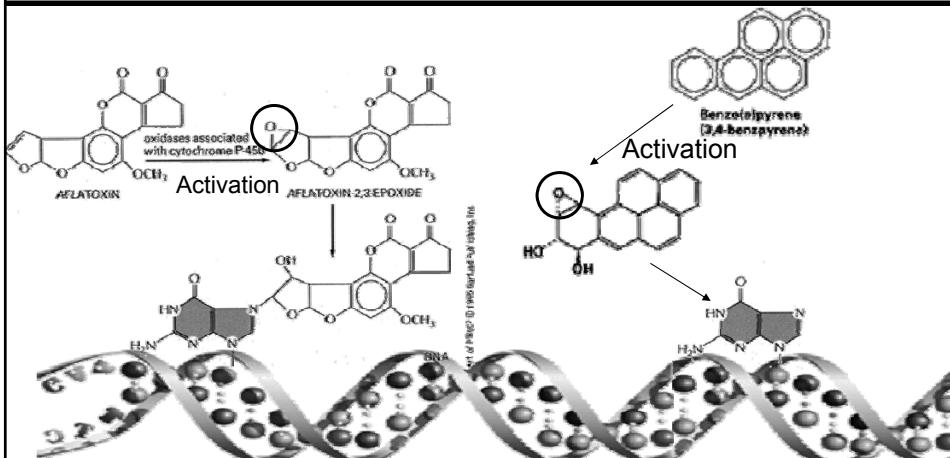
- Environmental procarcinogens are metabolized by cytochrome p450 enzymes
- Phytochemicals influence activities of phase I and phase II enzymes and thereby also metabolism of carcinogens

Metabolism of xenobiotics: environmental carcinogens, medical drugs and phytochemicals Phase I and II enzymes

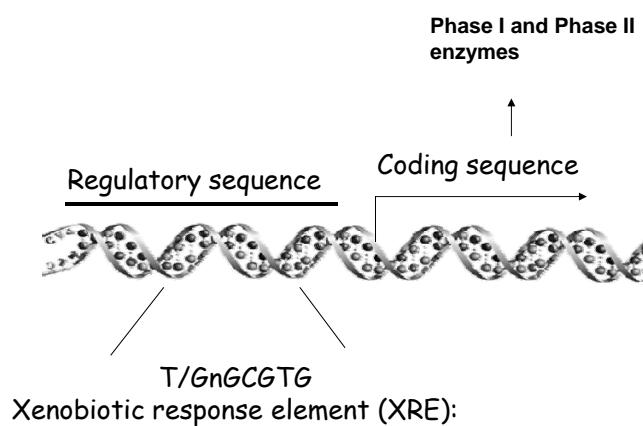


Metabolism of environmental carcinogenes

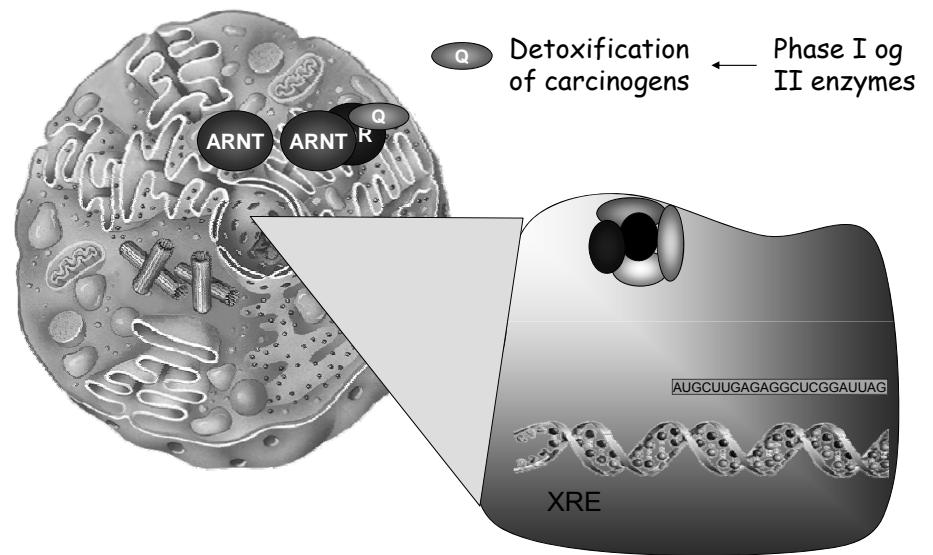
Formation of DNA adducts



Phytochemical regulation through xenobiotic response DNA element



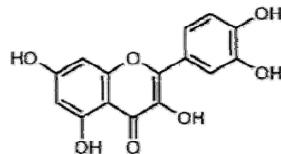
Phytochemicals in cytochrome p450 regulation



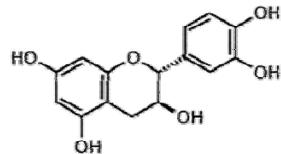
Cancer relevant effects of metabolism of xenobiotics/phytochemicals

- Positive effect:
 - Increase activity/amount of enzymes that inactivate procarcinogens
 - Inhibit activities of enzymes that activate procarcinogens
- Negative effect:
 - Increase activities of enzymes that activate procarcinogens
 - Inhibit activities of enzymes that inactivate procarcinogens

Phytochemicals in fruit, vegetables and berries (3 out of more than 8000 known)



quercetin
(flavonol)

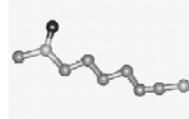


(+)-catechin
(flavonol)



Quercetin øker aktiviteten av fase I enzymer
Plasma koncentrasjonen etter et løkrikt måltid:
1 µM etter 0.7 timer

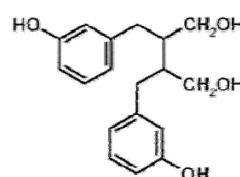
Phytochemicals in fruit, vegetables and berries (3 out of more than 8000 known)



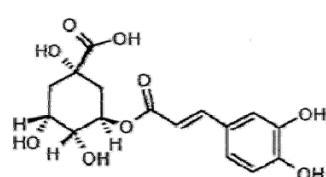
Sulforafan



Hemmer cytochrome P-450 2E1 som aktiverer prokarsinogener



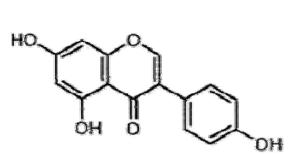
enterodiol
(lignan)



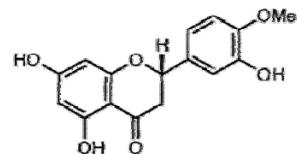
chlorogenic acid
(phenolic acid)



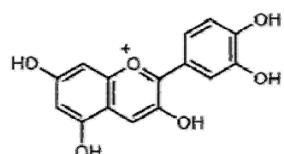
Phytochemicals in fruit, vegetables and berries (3 out of more than 8000 known)



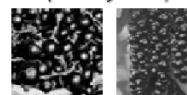
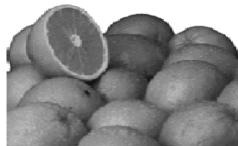
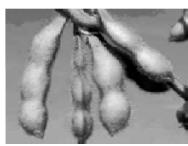
genistein
(isoflavone)



hesperetin
(flavanone)



cyanidin
(anthocyanidin)



Message:

Positive effects of phytochemicals that increase activity of procarcinogen-inactivating cytochrome P450s

Negative effects of phytochemicals that increase activity of procarcinogen-activating cytochrome P450s

Phytochemicals in pills

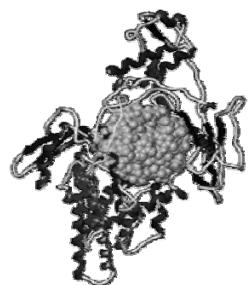


"Substances with effects always have side-effects"

Topoisomerase type II

Catalyse DNA double strandbreaks during DNA repair

Catalyse unwinding of DNA during DNA replication



Message:

**It is the combined effect
of a multitude of
phytochemicals in plant
derived food that reduces
cancer risk through many
mechanisms!**