1. **Master List Chemoprevention of Drugs and Natural Compounds for Cancer**

By James Watson

Attachment to blog entry **PART 3: *Slaying Two Dragons with the Sound of Silence.*** [***www.agingsciences.com***](http://www.agingsciences.com) **May 18, 2013**

**Source or Chemical Ingredients Mechanism of Action** **Cancer Effects with this Compound Anticancer Risk Reduction Dose w/this strategy**

**A** – **5α-reductase inhibitors**  (-) conversion of testosterone (-) prostate cancer 5mg qd (finasteride) 23%

Synthetic Examples: to dihydrotestosterone 0.5mg qd (dutasteride)

finasteride (+) apoptosis in prostate cancer cells

dutasteride

Natural Examples:

Green tea

Mushroom extracts (*Ganoderma lucidum)*

liposterolic extract of *Serenoa repens* (LSESr)

and β-sitosterol, in the treatment of AGA.

**Allspice extract** (*Pimenta dioca*) Ericifolin: silences AR in prostate CA anti-proliferative effects *in vivo* for breast 100-200 μg/ml *in vitro 50% ?*

ingredients: Eugenol, Gallic Epigenetic effect:` and prostate CA (55% in rodent model of

acid, and Ericifolin (-) HATs => (-) histone acetylation prostate CA and 52% in *in vivo* prostate

(histones H3 & H4 in promoter region of cancer cells.

AR gene and AR regulated genes

**Allyl mercaptan** (garlic)

Epigenetic mechanisms:

(-) HDACs

**Alprazolam** (see benzodiazepines) Epigenetic mechanisms:

BET bromodomain inhibiton

**Anastatins A & B**  Epigenetic mechanisms:u

(-) HDACs

**Anacardic acid** (see Epigenetic mechanisms

Cashew nut shell liquid) (-) HATs => NF-kB => LOX1

**Angiogenesis inhibitors** – see individual compounds listed elsewhere beneficial effects for prostate cancer, breast cancer,

naturally occuring: colorectal cancer, melanoma, and many other

emodin (*Oxygonum sinuatum)* (-) Protein kinase CK2 cancers in *in vitro, in vivo,* and in human clinical

coleon A lactone (*Plectranthus barbatus)* => (-)angiogenesis studies. Inhibition of angiogenesis alone does

Triphala churna (3 fruits) (-) VEGR-2 phosphorylation not have any effect, but when combined with

Vitamin E a cytotoxic chemotherapy regiment, increases

fish oil cancer inhibition and apoptosis via several

H2-blockers mechanisms, some of which may not involve

mushrooms angiogenesis

Curcumin

Cinnamon

Garlic

Spinach – chloroplast glycoglycerolipids

synthetic angiogenesis inhibitors epigenetic effects:

vorinostat (SAHA) – at low doses (-) HDACs

valproic acid – at low doses (-) HATs

**Apicidin** *(fungal metabolite)* (-) HDACs

**Aromatase inhibitors**  (-) Aromatase inhibits the proliferation of breast cancer

Synthetic:

Arimidex,

Femara

Natural:

Mushrooms

**Aspirin** (ASA) (-) Arachidonic acid cascade

(-) COX1 and COX2

(+) mTOR

**B – Bakuchi seed** (

**Berch Leaf** (

**Benzodiazepines** Epigenetic mechanisms:

examples: BET bromodomain inhibitors

alprazolam => selectively bind to acetyl lysine

midazolam modules of BET family

**B Vitamins** (primarily Folic acid (+) DNA methylation ⬇ risk of colon cancer

which has the anti-cancer effects) (+) stabilization of tumor suppressor genes => (-) LOH

**Bitter Melon Extract** (*Momordica charantia)* 5% solution in *in vivo*

Ingredients: (-) cell proliferation anti-cancer effects *in vitro* for breast cancer

charantin (+) apoptosis in cancer cells pancreatic cancer, nasopharyngeal cancer,

mormordin (+) cell cycle arrest and prostate cancer

& polyphenols

**Black Pepper**

**Blood Root** (

**Boswellic acid** (Frankincense) (-) topoisomerase I and II

(-) LOX

(+)Caspace and PARP cleavage

**3-Bromopyruvate** dual metabolic disruptor

(-) mitochondrial OxPhos

(-) hexose monophosphate pathway

**BET bromodomain inhibitors** (see Epigenetic mechanisms:

under names of individual compounds bind to acetyl lysine

listed below:) modules of BET family

JQ1 result: (-) c-Myc

iBET (triazolo-benzodiazepine)

alprazolam

midazolam

**Buckthrone bark**

**Butternut bark**

**Butyrate**  (+) AP-1 => paradoxical (-) of tumor growth

**C - Calcium** (-) fecal diacylglycerol => (-) cell proliferation ⬇ risk of colorectal polyps (adenomas)

**Cancer Stem Cell Apoptosis** (-) cell growth 100X more potent than paclitaxel in breast

salinomycin (+) induction of cancer stem cell differentiation cancer stem cells

(+) loss of cancer stem cell gene expression

**Chili Peppers** 200 mg/day

active ingredients:

capsaicin

capsicum

**Cashew nut shell liquid** Epigenetic mechanisms

ingredient: anacardic acid (-) HATs (p300) => (-) histone acetylation

(-) HATs => NF-kB => LOX1

**Celecoxib** (Celebrex) (-) COX2

(-) PDK1 => (-) mTOR

**Chapparral**

**Chia seeds**

**Coffee** (**Caffeic acid, aka CAFÉ,** (-) NF-kB => (-) COX2 ⬇ risk of colorectal aberrant crypt foci (ACF)

**and Chlorogenic acid**) (-) LOX

(+) HO-1

Epigenetic mechanisms

(-) HDACs

(-) DNMTs => (-) DNA demethylation

**Conjugated Linoleic acid (CLA)** 1 gm t.i.d.

(from Safflowers)

**Chlamydocin** (-) HDACs

**Cinnamon**

active ingredients:

Cinnamic acid (-) HDACs

hydroxycinnamic acid (-) HDACs

procyanidin oligomers (-) angiogenesis via VEGR-2

phosphorylation inhibition

**Cubeb berry**

**Curcumin** (see turmeric below)

**D** – **Vitamin D3**  (also known as (+) Klotho  ⬇ risk of breast cancer

1, 25-hydroxyviatamin D3) (-) angiogenesis ⬇ risk of colon cancer

**Diallyl disulfide**

**DFMO** (diflouromethylornithine) (-) ornithine decarboxylase (ODC) => (-) polyamine ⬇ risk of colorectal polyps (adenomas)

synthesis => (-) neoplasia

**Dragon blood**

**E** – **Vitamin E** (primarily (+) apoptosis in cancer cells with TNF-a ⬇ risk of breast cancer

α-tocopherol or α -TOS) (+) apoptosis in cancer cells with TNF-a ⬇ risk of colon cancer in animal models

(-) oncogenic Ras => (-) ERK signaling (-) angiogenesis

**EGCG, EGC** (see green tea below)

**Elesclomol** (+) apoptosis by generating ROS

**Equol** (-) HDACs

**Erucin** (sulforaphane analog) Epigenetic mechanisms:

(-) HDACs

**Eucalyptus leaf** (

**EVOO** (Extra virgin oive oil) (+) ER stress chaperones strong (-) of breast cancer cells

active ingredients: (+) Unfolded protein response genes EVOO secoiridoids prevent the epithelial

oleic acid (+) Heat shock proteins to mesenchymal transition (i.e. the

hydrophilic phenolics (+) ROS precancer-to-cancer conversion seens

lignans (+) CR mimetic in tumorigenesis that seems to be driven

flavonoids (+) c-Fos, c-Jun => (+) AP-1 => (+) polyamine by nearby senescent cells secreting

secoiridoids metabolism => (-) cancer the toxic inflammatory cytokines called

(+) AMPK the “senescence associated secretory

Epigenetic effects: phenotype” (SASP)

(+) SIRT1 => ⬇ MT genes, ⬇ Cancer stem cells

(-) cancer stem cell markers – SKP2 => less

degradation of tumor suppressors: p27, p57, p21, p130, FOXO1

(-) HATs

(+) spermidine upregulation (-) HATs

**F** – **Farnesol** HMGCoa feedback inhibitor

**Feverfew**

**Fiscetin**

**Fish Oil** (DHA & EPA) (-) oncogenic Ras => (-) ERK signaling ⬇ risk of colon cancer in animal models

(-) angiogenesis ⬇ risk of liver cancer

(+) immune effects  ⬇ risk of skin cancer

(-) endothelial cell adhesion

(-) Protein kinase B

**Flavones** (see polyphenols below)

**Flaxseed**

**Folic acid** (aka folate) methyl donor (deficiency can cause cancers) deficiency plays a role in breast, cervix,

(+) DNA repair ovary, brain, lung and colorectal

(+) DNA methylation

mechanism by which deficiency causes CA:

altered CpG methylation => (+) c-Myc activation

**Source or Chemical Ingredients Mechanism of Action** ⬇ **Cancer that This Compound**

**G** – **Gallic acid** (see Allspice)

**Garcinia** (Mangosteen fruit rind) (-) c-Myc => (+) apoptosis cytotoxic for leukemia, breast, gastric, 3-6 tablets/day of

ingredients: prenylated xanthones Epigenetic effects: lung and liver cancer *in vitro* 500-1000mg/tablet

and garcinol (-) HAT (p300 & PCAF) => (+) apoptosis

(-) HAT => (-) MAPK/ERK, PI3K/Akt, etc.

**Garlic** (see allyl mercaptan) (-) cell cycle progression

(+) apoptosis

(-) angiogenesis

Epigenetic effects

(-) HDACs => histone acetylation => apoptosis

**Green coffee beans** (-) nitrosylation of proline by nitrite ⬇ risk of environmental carcinogen-induced cancers

(Chlorogenic acid) (-) AP-1

(-) NF-kB

(-) MAPKs

Epigenetic Effects

(-) HDACs => (-) deacetylation of histones

(-) DNMTs => (-) DNA methylation

**Green tea** (-) COX2 => (-) PGE2 ⬇ risk of colon cancer in animal models & humans

(EGCG & EGC) (-) LOX ⬇ risk of pancreatic cancer in humans

(-) Topoisomerase ⬇ risk of prostate cancer, BPH, and alopecia

(+) apoptotic cancer cell death

(+) cell cycle arrest

(-) Telomerase

(-) 5α-reductase

(-) Skp2 => (-) tumor suppressor degradation

Epigenetic Effects

(-) HATs

(-) DNMTs

modulates miRNA

**Genistein** (see soybeans below) Epigenetic effects

(-) DNMTs =>

(-) HDACs

(+) HATs

modulates miRNA

**Gentisic acid** (-) FGF

found in: citrus fruits, grapes, artichoke,

sesame, red sandalwood, rose gum,

gentians, olive oil

**Goldenseal** (*Hydrastis Canadensis*) Antiproliferative bioactive herbs 2000mg/day Speranskia or goldenseal herb powder

**H – Histacin** (-) HDACs

**H2 blockers** (Cimetidine) (-) angiogenesis ⬇ risk of death from colon CA if taken preop

(and Ranitidine) (+) immune effect via IL-2 & IFN-α induction of NK cells & post op for 1 yr

(+) antigen presenting function of dendritic cells

(+) tumor infiltrating lymphocyte (TIL) activity

**Hydroxybenzoic acids**

found in: grapefruit, olive oil,

medlar fruit, carrots, oil

palm, grapes, red sandalwood,

peroba, betel palm, etc.

**I** – **Isothiocyanates** (+) Nrf2 => ARE genes => antioxidant enzymes ⬇ risk of colon cancer

found in: broccoli, brussel sprouts (-) HIF-1α => (-) VEGF, (-) LDH ⬇ risk of breast cancer

water cress (+) apoptosis ⬇ risk of prostate cancer

cauliflower and (-) hTERT

cabbage) Epigenetic mechanisms

6 natural compounds: (-) DNMTs => hypomethylates gene promoters

allyl isothiocyanate (-) HDACs =>  global and local

benzyl isothiocyanate histone acetylation

phenethyl isothiocyanate

sulforaphane

iberin

erucin – sulforaphane analog

Synthetic isothiocyanates

phenylhexyl isothiocyanate (-) HDACs => hypomethylates p16 => activation

p21 activation

**Isoflavones**

found in : soybeans, fava beans

and kudzu

**J** – **JQ1** (Brd4 inhibitor) Epigenetic mechanisms should reduce the risk of all c-Myc-driven

(-) BRD4 binding to chromatin cancers: multiply myeloma, leukemia,

(-) c-Myc => inhibition of cancer growth and lymphoma.

**K** – **Kochea seed** (-)

**L – Lanosterol** Feedback inhibitor of HMGCoA ⬇  aberrant crypt foci

**Lanperisone** (+) Apoptosis by generating ROS

**Lycopene, Luteolin, Lutein** (+) PPaR-γ ⬇ risk of prostate, lung, and breast cancer

(from tomatoes) (+) Nrf2 => ARE enzymes

**M – Mangostein fruit rind** (see Epigenetic effects: (-) HAT

Garcinia under G)

**Mahanine** (-) DNMTs => (-) DNA methylation

**Mayapple** *(Podophyllum peltatam)* (-) topoisomerase II FDA approved for lung cancer, choriocarcinoma, ovarian

active ingredient: cancer, testicular cancer, lymphoma, AML

etoposide

teniposide

**Metformin** (+) AMPK  ⬇ risk of colon, pancreatic, breast, prostate, lung, skin, and liver ca

(-) mTOR 25-35% cancer risk reduction overall

(+) Autophagy  55-62% risk reduction for pancreatic CA

**MitoQ** Metabolic disruptor

(-) Mitochondrial OxPhos

**Mushrooms** (+) lignin binding agents

(-) angiogenesis

(-) aromatase

**mTOR inhibitors**

natural compounds:

rapamycin

ECGC

curcumin

resveratrol

**Myrrh** (Sweet Myrrh)

**N** – **Nuts**

**NSAIDS** (aspirin, indomethacin, (-) COX2 => (-)PGE2 synthesis ⬇ risk of colon, pancreatic, breast, prostate, lung, skin, urinary ibuprofen, and COX2 specific (-) LOX bladder, and liver cancers

inhibitors like Celebrex) (+) AMPK  total risk ⬇ for breast cancer may be as high as 40-50%, primarily via (-) COX2

**O** – **Olive oil** (see also EVOO,

secoiridoids, and n-Tyrosol) (+) ER stress chaperones strong (-) of breast cancer cells

active ingredients: (+) Unfolded protein response genes

oleic acid (+) Heat shock proteins

hydrophilic phenolics (+) ROS

lignans (+) CR mimetic

flavonoids (+) c-Fos, c-Jun => (+) AP-1 => (+) polyamine

secoiridoids metabolism => (-) cancer

N-tyrosol Epigenetic effects:

Hydroxytyrosol (+) SIRT1 => ⬇ MT genes, ⬇ Cancer stem cells

(-) cancer stem cell markers – SKP2 => less

degradation of tumor suppressors: p27, p57, p21, p130, FOXO1

(-) HATs

**Onions**

**Osho root**

**Oxaloacetate** *(Eunonymous alata)*(+) FOXO1 and FOXO3  lifespan in model organisms by 15-25% 100mg – 1,000mg/day

also known as “burning bush” (+) AMPK (-) lung cancer *in vitro*

(-) MMP-9 => (-) tumor metastisis

(+) Mitochondrial DNA protection

**P – Parthenolide** (-) DNMT

**Phytannic acid**

**Piperlongumine** (-) selective apoptosis in cancer cells

**(***Piper Longum* extract via blockage of antioxidant enzymes

**Plumbagin** (see Venus (-) HATs inhibited the transition from IEN to poorly differentiated CA

Flytrap extract and (-) NF-kB binding to DNA in prostate cancer animal model (75%)

also see Walnuts) (-)AP-1 binding to DNA inhibited UV-induced development of squamous cell CA when

(-) STAT3 binding to DNA applied topically in animal model of SCCA

(-) anti-apoptotic factors

(-) cell cycle progression

(+) apoptosis via PARP cleavage, etc.

(-) ROS-induced apoptosis

**Polyphenols** (-) Nrf2 ⬇ risk of oral, breast, prostate, gastric, ovarian

Sources: Epigenetic mechanisms esophageal, skin, colorectal, pancreatic, and

Dietary:fruits,vegetables, olive oil (-) DNMTs => prevents or reverses head and neck cancer

Drinks – tea, wine hypermethylation of tumor suppressor

Botanicals – (> 1,000) gene promoter sites

10 classes:

flavonoids

stilbenes

phenolic acids

benzoquinones,

acetophenones

lignins

xanthones

**Pyruvate**  6 gms/day for 2

months at a time

**Q – Quercetin** (red apples) (-) PI3K

Epigenetic effects

(-) DNMT => (-) DNA methylation

**R** – **Rapamycin** (-) mTOR

(+) Autophagy

**Red Sandalwood oil** *(Santalum album)*

active ingredients:

1. pterostilbene – natural (-) COX-1

analog of reseveratrol (-) NF-kB

2. α-santalol (+) apoptosis via Caspace activation

(+) PARP cleavage

(+) mitochondrial membrane disruption

**Resveratrol** (also known (+) Nrf2

as (+) SIRT ⬇ risk of colon, liver, skin, breast, prostate

sources: red grape skins, wine (+) cell cycle arrest in cancer cells and lung cancer

peanuts, mulberries (-) aromatase (better with resveratrol analogs)

cranberries, japanese (-) quinone reductase 2 (QR2) – better with resveratrol analogs

knotweed (-) COX2

(-) NF-kB

(+) AMPK

(+) glucocorticoid receptor activation

Epigenetic mechanisms

(-) DNMTs – not as strong as green tea, however

(-) HDACs

(+) SIRT-1

**Rosemary Leaf** (*Rosmarinus Oficinalis)*  cytotoxic for ALL, colon, and breast cancer

active ingredient: camosol

**S** – **Safflower** (see conjugated linoleic acid, aka CLA)

**Sage**

**SAHA** (Vorinostat) (-) HDACs

**Salicylate** (natural, non-acetylated (+) AMPK

form of aspirin)

**SARMs (**Selective Androgen Receptor

Modulators – SARMs)

**Secoiridoids** (olive oil hydrophilic (+) resveratrol-like gene activation

phenolics, and other olive oil (+) ER UPR – DnaJ, ERdj, etc.

derived compounds) (+) mitochondrial UPR – GADD153, Chop, etc.

(+) Heat shock proteins – Hsp70B, Hsp72, Hsp70t, etc.

(+) c-Fos and polyamine metabolism

(+) c-Jun => (+) AP-1 => paradoxic (-) cancer growth

(+) polyamine synthesis => (+) spermidine => (-) HATs

(+) polyamine catabolism => (-) tumor cell growth

(+) SIRT1

(-) metallothionein (MT) => metal ion homeostasis

=> (-) tumorigenesis and (-) cancer stem cells

(-) ALDH1A3 gene => (-) cancer stem cells

(-) Skp2 => (-) UPS for degrading tumor suppressor

proteins – p27, p57, p21, FOXO1

(-)LDHA => (-) lactate dehydrogenase => (-) Warburg effect

**Selenium** Epigenetic mechanism ⬇ risk of prostate cancer and lung cancer

sources: Brazil nuts (-) DNMTs => ⬇ aberrant crypt foci in the colon and colon polyps

chicken, game meat (-) HDACs

beef, garlic

**Senna leaf**

**Soybeans** (Genistein, soyasaponins) (-) protein tyrosine kinases ⬇ risk of colon, breast, and prostate cancer

(-) TGF-beta1

(+) NAG-1 => 50% reduction in proliferation

& 6X increase in apoptosis in cancer cells

Epigenetic Mechanisms of Action

(-) HDACs => (-) deacetylation of histones

(-) DNMT => (-) DNA methylation

(+) HATs

modulates miRNA

**Statins** examples: (-) Lymphocyte-function associated antigen epidemiologic studies show risk of Colon CA and melanoma

Lovastatin (+) miR-33a & b => ⬇ c-Myc expression c-Myc is the most common abnormality found in cancer Atorvastatin (-) geranylgeranylation=>(-)Rho proteins) statins should inhibit all c-Myc up regulated cancers

Mevastatin risk reduction of colon cancer 30-67% in animal models

13-17% risk reduction of colon cancer in epidemiologic studies

10-33% risk reduction of breast cancer in epidemiologic studies

19-37% risk reduction of melanoma in epidemiologic studies

13-63% risk reduction of prostate cancer in epidemiologic studies

0-28% risk reduction for cancer overall in epidemiologic studies

**Squalene** (-) inhibits colon aberrant crypt foci

**T – Tamoxifen**

**Trapoxin** (-) HDACs

**Triphala churna** – made from (-) angiogenesis by (-) VEGR-2 (-) growth of stomach cancer, lymphoma, and pancreatic CA

3 fruits: *Emblica ooficinalis* phosphorylation

*Terminalia chebula*

*Terminalia belerica*

primary active ingredients:

chebulinnic acid

**Turmeric** (Curcumin) (-) NF-kB => (-)COX2, LOX, NOS, MMP-9, uPA,TNF  ⬇ risk of colon cancer with natural curcumin.

(-) AP-1  ⬇ risk of gastric cancer

(-) Egr-1

(-) JNK

(-) STATs => (-) anti-apoptotic proteins

(-) angiogenesis

(-) cytochrome P450

(+) cell cycle arrest

(+) apoptosis of cancer cells via Caspace activation

(-) β-catenin

(-) PhKinase

Epigenetic Mechanisms of Action

(-) HDAC 1,3, and 8 - curcumin given before docetaxel may increase

(+) HDAC 2 breast cancer response rate to docetaxel via an

(-) HATs => (-) acetylation of p53, epigenetic mechanism

RelA (NF-kB), and GATA4 - curcumin given before gemcitabine may increase

(-) DNMTs => DNA methylation pancreatic cancer susceptibility to gemcitabine

(+) miR-22 expression => 50 downstream targets

(-) miR-186 expression

**U** – **Ursolic acid**

**V – Venus Flytrap extract** (*Plumbago rosea)*

active ingredients: (-) AP-1 anti-cancer effects have been shown *in vitro* 30 drops of Carnivora /3-5X/day

plumbagin Epigenetic effects but there is no clinical studies to support this claim or 125 μg capsules – 6-9 caps/day

flavanoids (-) HDACs

**Vitamin A (**Retinoids) (-) PKC ⬇ risk of colon cancer

**Vitex** (*Vitex Agnus-Castus)* (+) Caspace induction => ⬇ Bcl-2, cytotoxic for ovarian, cervical, breast 30-40mg/day

⬇ Bcl-XL, Bid, Bad gastric, colon, and lung CA *in vitro*

**VOAS** (Volatile oil if *Radix A. sinensis)*  (-) angiogenesis 30-50 μg/ml

active ingredient: *n-*butylidenephthalide (-) platelet aggregation

**W** – **Walnuts**

active ingredients:

plumbagin inhibits hormone refractory prostate cancer *in vitro*

**Wild cherry bark** (*Prunus Serotina)* (-) Cyclin D1

(+) apoptosis via (+) NAG-1 gene

(-) β-catenin

**Wild Yam** (Dioscorea Villosa) (-) cell cycle arrest

ingredients: diosgenin (-) NF-kB, Akt, Cyclin D, c-myc

(+) apoptosis

**Wine** (red and white)

active ingredients

red - resveratrol (+) SIRT1, (+) AMPK

white – n-tyrosol (+) FOXO3

and hydroxytyrosol (+) FOXO3

**Xanthines** (-) mTOR

examples: (-) PDE

caffeine (-) TNF-α

theobromine (chocolate) (-)leukotriene synthesis

theophylline

**Y – Yellow dock root**

**Yerba mate**

active ingredients (-) mTOR

caffeine (-) PDE

theobromine (-) TNF-α

theophylline (-)leukotriene synthesis

**Z – Zerumbone** (-) HDACs

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