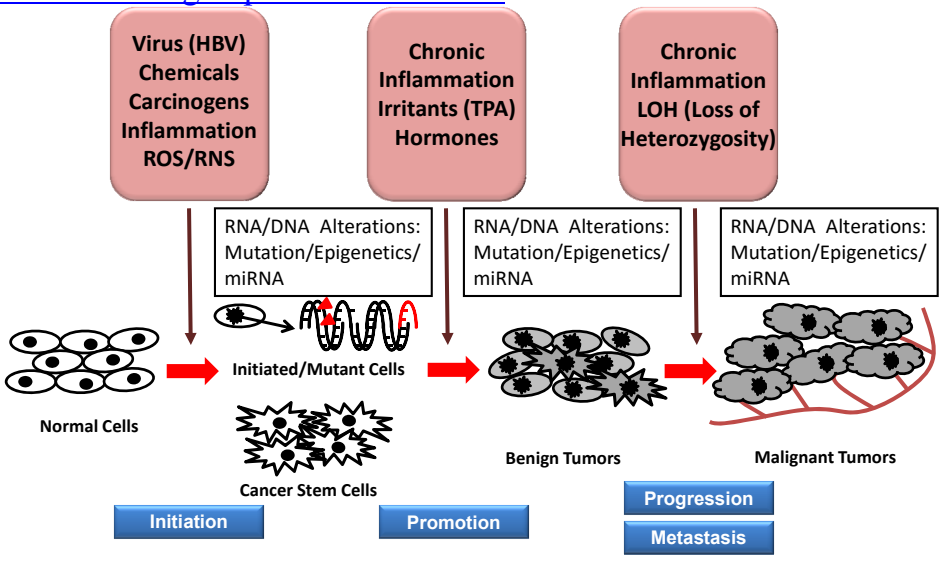
Research from Professor Ah-Ng Tony Kong's Laboratory

Professor Kong's current research involves Pharmacodynamics of dietary phytochemicals; Cancer interception/prevention by dietary phytochemicals, botanical products, and drugs/repurposed drugs; Human pharmacokinetics (PK)/pharmacodynamics (PD) studies and PKPD modeling and simulation; NRF2-mediated Redox Signaling; Mitochondrial metabolic and epigenetic reprogramming in diseases and phytochemicals/drug treatments. The impact of Professor Kong's research reflected by more than 300 publications with a total citation of more than 36,000, *H*-Index of 109 and trained more than 80 doctoral students, postdoctoral associates, and visiting scholars with 30 NIH R01 grants being funded to date.

Cancers are Preventable Diseases: Cancer Prevention by Dietary Phytochemicals and NSAIDs

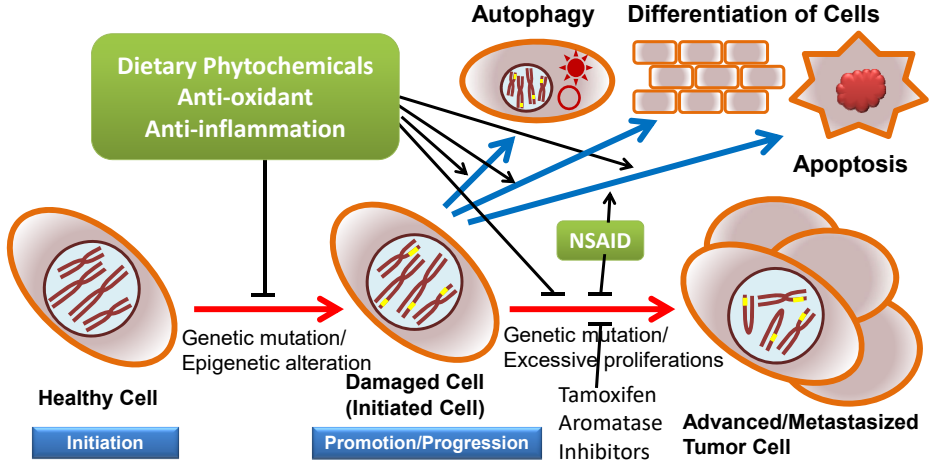
Cancer development generally involves multi-stage processes including initiation, promotion and progression (scheme below). In human, depending on the organs/tissues, cancer takes between 10 to 50 years from the initiation stages to diagnosable stages and to advanced metastisized stages of tumors. Evidence suggests that ~80% of human cancers are linked to environmental factors impinging upon genetics/epigenetics. Recent evidence suggests that adults younger than 50, there is an increase in overall cancer incidence from 1995 to 2020 (*CA Cancer J Clin*. 2024;74(1):12-49). This implicates that high risk exposure to environmental factors such as dietary factors, among others, in earlier years (eg in their 20s), would see an increase cancer rates in their 30s or 40s.

Since advanced metastasized cancers often time are resistant to radiation/chemotherapeutic drugs, cancer prevention of earlier stages of cancers with healthy diets, exercise, abstence of smoking and heavy alcohol consumption, among others, and for "high risk individuals" by relatively non-toxic pharmacological doses of dietary cancer preventive phytochemicals or drugs will be logical (*Cancer Prev Res (Phila)*. 2021 Feb;14(2):151-164). During cancer development peroid, there are windows of opportunity to block and intercept the progression of cancer using relatively non-toxic dietary phytochemicals and or NSAIDs (such as aspirin) (scheme below). ***Reference***: "Dietary phytochemicals and cancer prevention: Nrf2 signaling, epigenetics, and cell death mechanisms in blocking cancer initiation and progression." Lee JH, Khor TO, Shu L, Su ZY, Fuentes F, **Kong AN**. *Pharmacol Ther.* 2013 Feb;137(2):153-71. doi: 0.1016/j.pharmthera.2012.09.008. Epub 2012 Oct 3. http://www.ncbi.nlm.nih.gov/pubmed/23041058.



Schematic representation of multi-stage carcinogenesis

Exposure to intrinsic/extrinsic factors, including various toxic chemicals, oncogenes, viruses (e.g., HBV, hepatitis B virus), ROS/RNS, and inflammation, can resulting in genetic mutations and/or epigenetic alterations that cause the initiation of carcinogenesis in normal cells. The initiated cells and non-neoplastic cancer stem/progenitor cells can first progress to benign tumors, which would be amendable with surgery, radiation and or chemotherapy, if detected early, with subsequent progression to advanced/metastasized/malignant/drug-resistant tumors due to the prolonged effects of chronic inflammation, various irritants and aberrant hormones. Advanced/metastasized/malignant tumors are typically very difficult to treat since they are resistant to radiation and chemotherapy. Hence it is critically important to **PREVENT** cancers from progressing to the latter stages.

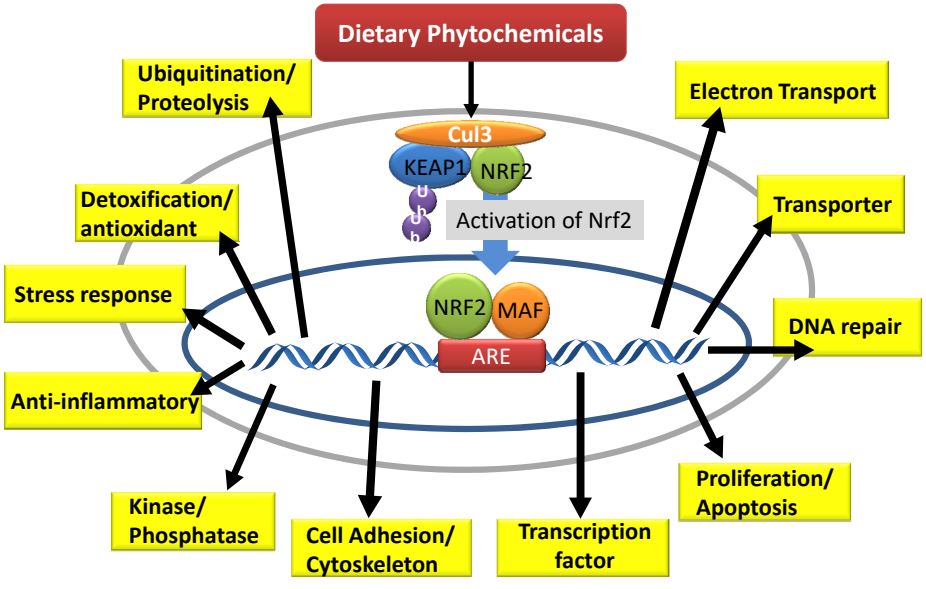


Schematic representation of cancer chemoprevention strategy using dietary phytochemicals and non-toxic therapeutic drugs

Oxidative stress, inflammation and reactive intermediates of carcinogens can cause genetic mutations and epigenetic alterations. Through the promotion/progression stages, initiated cells become advanced/ metastatic tumor cells. Applying dietary phytochemicals at the early stage of carcinogenesis may block further development of carcinogenesis. Treatment with dietary phytochemicals and/or relatively non-toxic therapeutic drugs on cancer cells may induce positive results, including autophagy, cell cycle arrest, apoptosis, and differentiation, and may block tumor development.

Cancer Prevention by Dietary Phytochemicals via NRF2-signaling Pathway

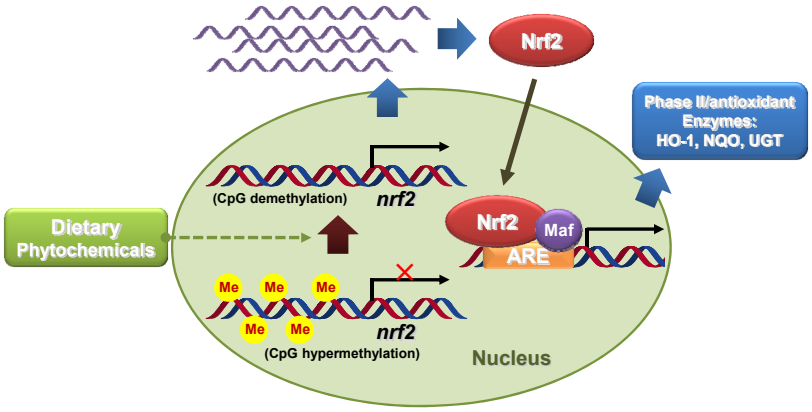
Nrf2 is a master regulator of anti-oxidative stress and anti-inflammatory responses. Surprisingly, many health beneficial/anti-cancer dietary phytochemicals found abundantly in our fruits, vegetables, nuts, among others, would activate Nrf2 resulting in induction of cellular defense detoxifying/antioxidant enzymes and inhibition of inflammatory responses in many tissues. Consequently, Nrf2 appears to be a critical factor/ biomarker in cancer development and cancer prevention. http://www.ncbi.nlm.nih.gov/pubmed/23041058; http://www.ncbi.nlm.nih.gov/pubmed/22836898; http://www.ncbi.nlm.nih.gov/pubmed/20486765



Epigenetics, Epigenomics and Cancer Prevention

As discussed above, cancer is driven by a series of genetic/epigenetic changes in tumor suppressor genes and oncogenes impacted in part by oxidative stress, inflammatory signals, among others. The concept of epigenetics has been defined as "the study of heritable changes in gene expression that occur without a change in DNA sequence" (Wolffe et al., 1999). In cancer, epigenetic hypermethylation of the promoter regions of certain tumor suppressor genes is thought to be the most relevant epigenetic change associated with malignant transformation. These heritable changes occur through the methylation of cytosine bases in the DNA and by post-transcriptional modifications of histones (Baylin et al., 2000).

Environmental factors, diet and lifestyle have an impact on the development of various cancers in humans. Hence, minimizing exposure to environmental carcinogens, maintaining a healthier lifestyle (eg exercise) and consuming a healthy diet are thought to be reasonable approaches for cancer prevention. In addition to genetic mutations, epigenetic alterations play an important role in cancer development. It is believed that epigenetic changes arise before genetic alterations. The potential of dietary phytochemicals as cancer chemo-preventive/anti-cancer agents through epigenetic modification has been demonstrated in many studies. http://www.ncbi.nlm.nih.gov/pubmed/23041058; http://www.ncbi.nlm.nih.gov/pubmed/21938566; http://www.ncbi.nlm.nih.gov/pubmed/21787756; http://www.ncbi.nlm.nih.gov/pubmed/22457388; http://www.ncbi.nlm.nih.gov/pubmed/23416117; http://www.ncbi.nlm.nih.gov/pubmed/23441843



Dietary phytochemicals like sulforaphane, curcumin, triterpenoids, among others would drive epigenetics reprogramming potentially resulting in cancer and health protection.

References:

Pharmacodynamics of curcumin as DNA hypomethylation agent in restoring the expression of Nrf2 via promoter CpGs demethylation. *Biochem Pharmacol*. 2011

Sulforaphane enhances Nrf2 expression in prostate cancer TRAMP C1 cells through epigenetic regulation. *Biochem Pharmacol*. 2013 Feb 14.

A gamma-tocopherol-rich mixture of tocopherols maintains Nrf2 expression in prostate tumors of TRAMP mice via epigenetic inhibition of CpG methylation. *J Nutr*. 2012 May;142(5):818-23.

The epigenetic effects of aspirin: the modification of histone H3 lysine 27 acetylation in the prevention of colon carcinogenesis in azoxymethane- and dextran sulfate sodium-treated CF-1 mice. *Carcinogenesis*. 2016

Epigenetic modifications of triterpenoid ursolic acid in activating Nrf2 and blocking cellular transformation of mouse epidermal cells. *J Nutr Biochem*. 2016 Jul;33:54-62.

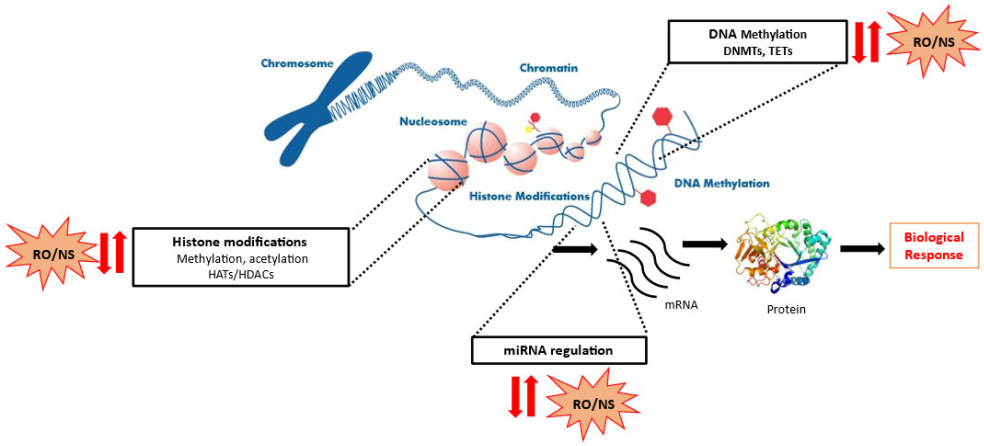
CpG methyl-seq and RNA-seq epigenomic and transcriptomic studies on the preventive effects of Moringa isothiocyanate in mouse epidermal JB6 cells induced by the tumor promoter TPA. *J Nutr Biochem.* 2019 Jun;68:69-78. doi: 10.1016/j.jnutbio.2019.03.011. Epub 2019 Mar 28.

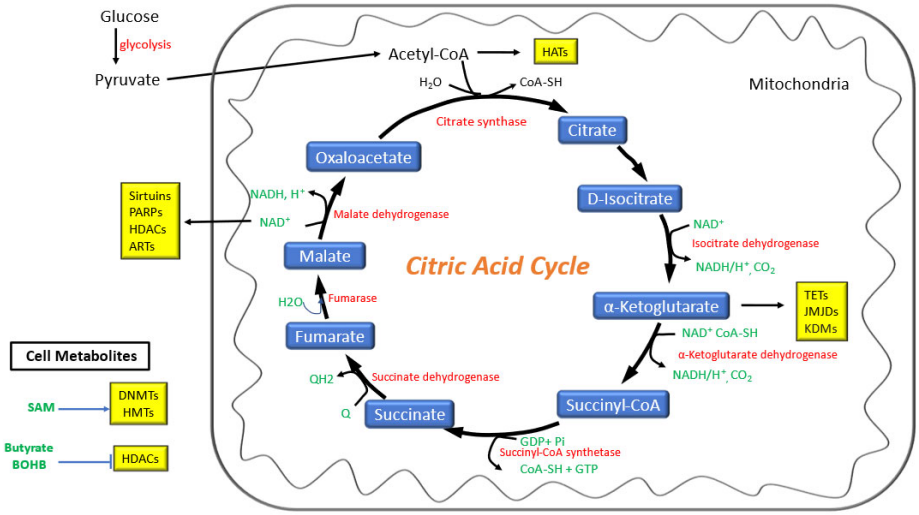
Anthocyanin Delphinidin Prevents Neoplastic Transformation of Mouse Skin JB6 P+ Cells: Epigenetic Re-activation of Nrf2-ARE Pathway. *AAPS J*. 2019 Jun 28;21(5):83.

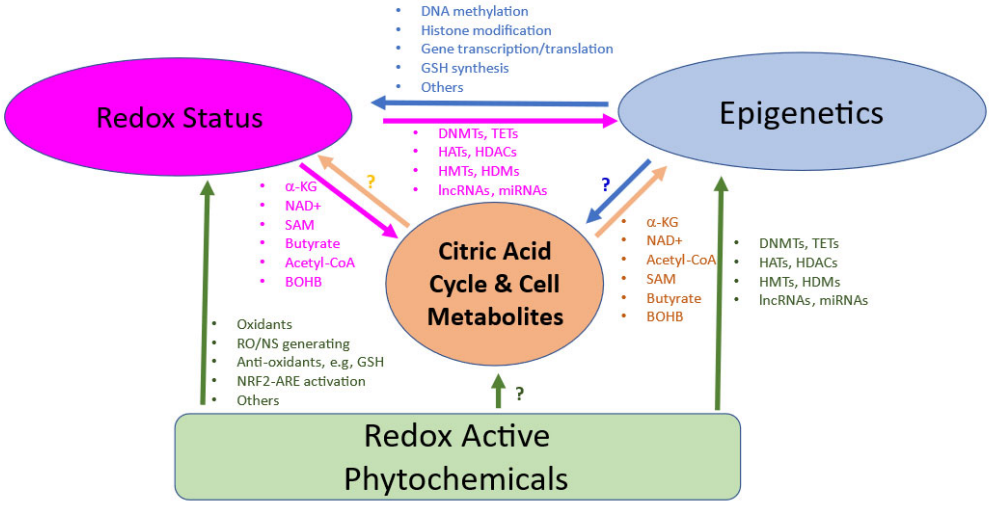
Epigenetics/Epigenomics and Prevention of Early Stages of Cancer by Isothiocyanates. *Cancer Prev Res (Phila)*. 2021 Feb;14(2):151-164.

Redox Signaling, Epigenetic, and Metabolic Reprogrammming in Carcinogenesis and prevention by dietary anti-cancer phytocchemicals

Biological redox signaling plays an important role in many diseases including cancer (Redox Signaling, mitochondrial metabolism, epigenetics and redox active phytochemicals. *Free Radic Biol Med.* 2022). Recent evidence suggests that reactive oxygen/nitrogen species (RO/NS) modulate epigenetic machinery driving gene expression. RO/NS affect DNA methylation/ demethylation, histone acetylation/deacetylation or histone methylation/demethylation. Many health beneficial phytochemicals possess redox capability that counteract RO/NS either by directly scavenging the radicals or via inductive mechanism of cellular defense antioxidant/reductive enzymes. Amazingly, these phytochemicals also possess epigenetic modifying ability. Graphical presentations as summarized below.







Recently, Professor Kong's lab integrated research on mitochondrial metabolic rewiring, epigenetic reprogramming, transcriptomic gene expression and redox activators dietary anti-cancer phytochemicals to better understand cancer progression and prevention/treatment. We found that redox signaling plays an important role in the rapid metabolic rewiring of critical metabolic pathways including the tricarboxylic acid (TCA) in sensing the cellular microenvironment redox status by rewiring some of the metabolites including Acetyl Coenzyme A, α-ketoglutarate, NAD+, S-adenosyl methionine (SAM) which are co-factors of the basic epigenetic machinery driving epigenetic reprogramming. Mitochondrial metabolites also provide bioenergetics to support cell growth.

References:

UVB drives different stages of epigenome alterations during progression of skin cancer. *Cancer Lett.* 2019

DNA methylome and transcriptome alterations and cancer prevention by triterpenoid ursolic acid in UVB-induced skin tumor in mice. *Mol Carcinog*. 2019

Tobacco carcinogen 4-[Methyl(nitroso)amino]-1-(3-pyridinyl)-1-butanone (NNK) drives metabolic rewiring and epigenetic reprograming in A/J mice lung cancer model and prevention with Diallyl Sulphide (DAS). *Carcinogenesis*. 2021

Pten-knockout regulates metabolic rewiring and epigenetic reprogramming in prostate cancer and chemoprevention by triterpenoid ursolic acid. *FASEB J.* 2022

The environmental carcinogen benzo[a]pyrene regulates epigenetic reprogramming and metabolic rewiring in a two-stage mouse skin carcinogenesis model. *Carcinogenesis.* 2023

Butyrate Drives Metabolic Rewiring and Epigenetic Reprogramming in Human Colon Cancer Cells. *Mol Nutr Food Res*. 2022

Triterpenoid ursolic acid regulates the environmental carcinogen benzo[a]pyrene-driven epigenetic and metabolic alterations in SKH-1 hairless mice for skin cancer interception. *Carcinogenesis.* 2024 Mar 11.

Pharmacokinetics-Pharmacodynamics and PKPD Modeling

Professor Kong developed an interest in Pharmacokinetics (PK)-Pharmacodynamics (PD) and PKPD modeling and simulation when he was a PhD student with Professor William J. Jusko; a world renown PKPD scientist, in the 1980s. While in Professor Jusko's lab, he developed one of the first generation of Indirect Response (IDR) PKPD model "Pharmacokinetics and pharmacodynamic modeling of direct suppression effects of methylprednisolone on serum cortisol and blood histamine in human subjects". Kong AN, Ludwig EA, Slaughter RL, DiStefano PM, DeMasi J, Middleton E Jr, Jusko WJ. Clin Pharmacol Ther. 1989 Dec;46(6):616-28. Subsequently, Professor Kong has been continuing working on PKPD studies and modeling of the blood concentrations of dietary phytochemicals and their corresponding pharmacodynamic responses/pharmacological effects.

References:

Pharmacokinetics and pharmacodynamics of phase II drug metabolizing/antioxidant enzymes gene response by anticancer agent sulforaphane in rat lymphocytes. *Mol Pharm*. 2012.

Pharmacokinetics and pharmacodynamics of 3,3'-diindolylmethane (DIM) in regulating gene expression of phase II drug metabolizing enzymes. *J Pharmacokinet Pharmacodyn*. 2015.

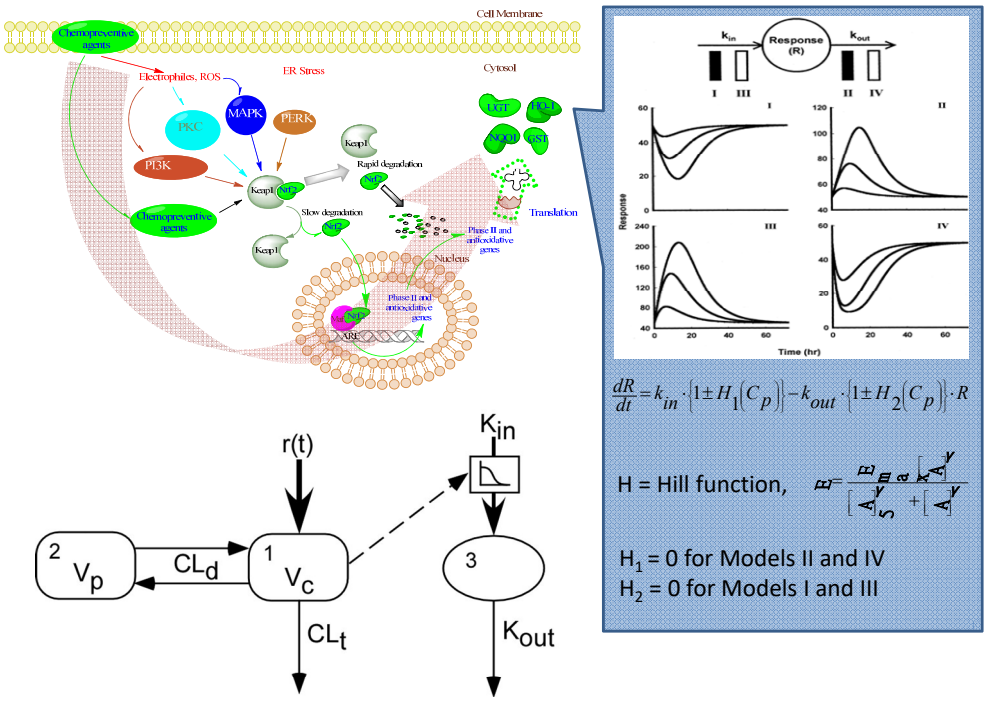
Pharmacokinetics and Pharmacodynamics of the Triterpenoid Ursolic Acid in Regulating the Antioxidant, Anti-inflammatory, and Epigenetic Gene Responses in Rat Leukocytes. *Mol Pharm.* 2017 Nov 6;14(11):3709-3717.

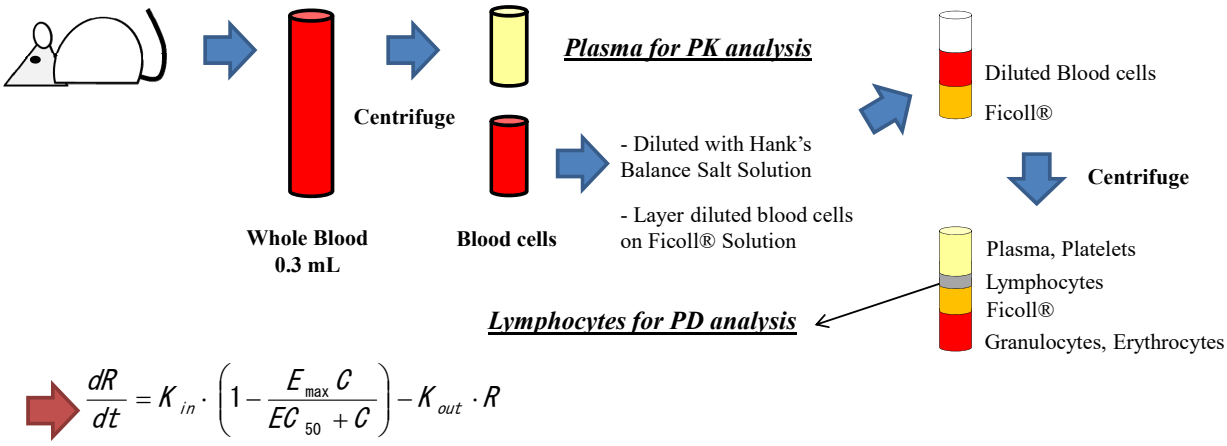
Pharmacokinetics and Pharmacodynamics of Curcumin in regulating anti-inflammatory and epigenetic gene expression. *Biopharm Drug Dispos.* 2018 Jun;39(6):289-297.

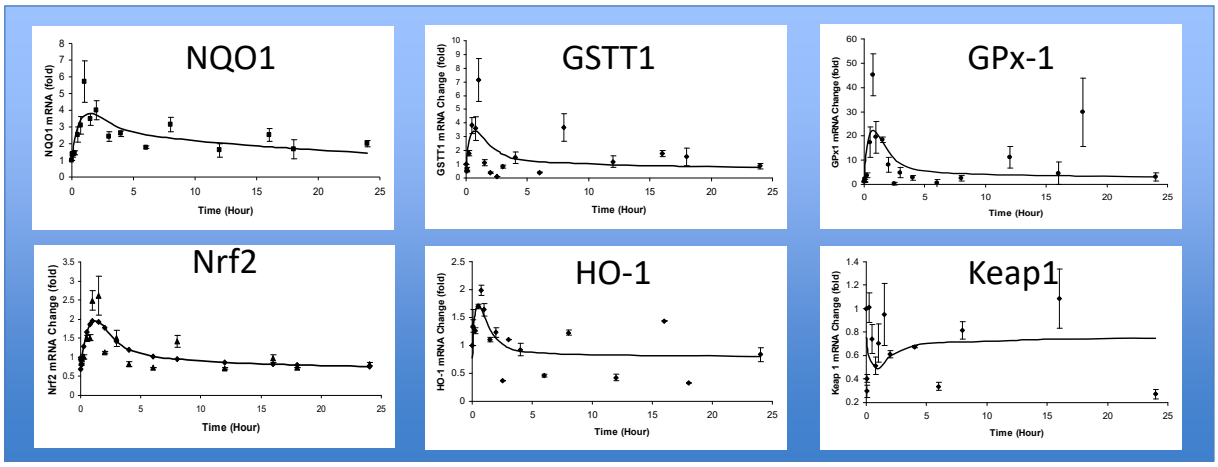
Pharmacokinetics, Pharmacodynamics, and PKPD Modeling of Curcumin in Regulating Antioxidant and Epigenetic Gene Expression in Healthy Human Volunteers. *Mol Pharm*. 2019.

Pharmacokinetics and Pharmacodynamics of Anthocyanins after Administration of Tart Cherry Juice to Individuals with Gout. *Mol Nutr Food Res*. 2023.

http://www.ncbi.nlm.nih.gov/pubmed/22931102; https://pubmed.ncbi.nlm.nih.gov/30860383/







[**Pharmacokinetics** and Pharmacodynamics of Anthocyanins after Administration of Tart Cherry Juice to Individuals with Gout.]
Brunetti L, Wang L, Wassef A, Gong Y, Brinker A, Buckley B, Lipsky PE, Ondar P, Poiani G, Zhao L, **Kong AN**, Schlesinger N. Mol Nutr Food Res. 2023 May;67(9):e2200550. doi: 10.1002/mnfr.202200550. Epub 2023 Mar 12. PMID: 36843307 Clinical Trial.
METHODS AND RESULTS: This study aims to quantitate the major anthocyanins in TC Juice Concentrate (TCJC) and identify the pharmacokinetic (**PK**) and pharmacodynamic (**PD**) parameters of the major anthocyanin cyanidin-3-glucosylrutinoside (C3GR). A **PK-PD** st …

[**Pharmacokinetics** and pharmacodynamics of three oral formulations of curcumin in rats.]
Wang L, Li W, Cheng D, Guo Y, Wu R, Yin R, Li S, Kuo HC, Hudlikar R, Yang H, Buckley B, **Kong AN.** J Pharmacokinet Pharmacodyn. 2020 Apr;47(2):131-144. doi: 10.1007/s10928-020-09675-3. Epub 2020 Feb 4. PMID: 32020381 Free PMC article.
The purpose of this preclinical study is to investigate the acute pharmacokinetic and pharmacodynamic (**PK**/**PD**) profiles of two commercially marketed CUR products (GNC and Vitamin Shoppe) and a CUR powder from Sigma in female rats. ...Physiologically based **PK** m …

[**Pharmacokinetics**, Pharmacodynamics, and PKPD Modeling of Curcumin in Regulating Antioxidant and Epigenetic Gene Expression in Healthy Human Volunteers.]
Cheng D, Li W, Wang L, Lin T, Poiani G, Wassef A, Hudlikar R, Ondar P, Brunetti L, **Kong AN.** Mol Pharm. 2019 May 6;16(5):1881-1889. doi: 10.1021/acs.molpharmaceut.8b01246. Epub 2019 Mar 28. PMID: 30860383 Free PMC article.

The purpose of this clinical study is to describe the acute **pharmacokinetics** and pharmacodynamics (**PK**/**PD**) of commercially marketed curcumin in normal, healthy human volunteers. ...COG **PK** is well-described by a one-compartment model, and the **PK**/ …

Pharmacokinetics and Pharmacodynamics of Curcumin in regulating anti-inflammatory and epigenetic gene expression.
Boyanapalli SSS, Huang Y, Su Z, Cheng D, Zhang C, Guo Y, Rao R, Androulakis IP, **Kong AN.** Biopharm Drug Dispos. 2018 Jun;39(6):289-297. doi: 10.1002/bdd.2136. PMID: 29870054 Free PMC article.
While the anti-oxidant and anti-inflammatory effects of curcumin, a natural product present in the roots of Curcuma longa have been studied widely, the acute **pharmacokinetics** (**PK**) and pharmacodynamics (**PD**) of curcumin in suppressing pro-inflammatory markers a …

A Novel Triple Stage Ion Trap MS method validated for curcumin **pharmacokinetics** application: A comparison summary of the latest validated curcumin LC/MS methods.
Li W, Yang H, Buckley B, Wang L, **Kong AN.** J Pharm Biomed Anal. 2018 Jul 15;156:116-124. doi: 10.1016/j.jpba.2018.04.022. Epub 2018 Apr 17. PMID: 29702389 Free PMC article.
The linear calibration curve for quantifying curcumin in rat plasma was 1-3000 ng/ml ($r(2) > 0.99$) with intra-day and inter-day RSD and accuracy within 5.11%. Its application in a **Pharmacokinetics** (**PK**) study demonstrated detection of curcumin at a very low plasma …

Pharmacokinetics and Pharmacodynamics of the Triterpenoid Ursolic Acid in Regulating the Antioxidant, Anti-inflammatory, and Epigenetic Gene Responses in Rat Leukocytes.
Zhang C, Wang C, Li W, Wu R, Guo Y, Cheng D, Yang Y, Androulakis IP, **Kong AN.** Mol Pharm. 2017 Nov 6;14(11):3709-3717. doi: 10.1021/acs.molpharmaceut.7b00469. Epub 2017 Oct 25. PMID: 29035547 Free PMC article.
The **PK-PD** model provided reasonable fitting linking the plasma concentration of UA simultaneously with the **PD** response based on leukocyte mRNA expression. Overall, our results indicate that UA is effective at inducing various phase II DM/antioxidant genes and …

Pharmacokinetics and pharmacodynamics of 3,3'-diindolylmethane (DIM) in regulating gene expression of phase II drug metabolizing enzymes.
Wu TY, Huang Y, Zhang C, Su ZY, Boyanapalli S, Khor TO, Wang H, Lin H, Gounder M, Kagan L, Androulakis IP, **Kong AN.** J Pharmacokinet Pharmacodyn. 2015 Aug;42(4):401-8. doi: 10.1007/s10928-015-9421-5. Epub 2015 Jul 3. PMID: 26138223
3,3'-Diindolylmethane (DIM) has been investigated as a potential anti-cancer chemopreventive agent in many preclinical and clinical studies. In this study, we sought to characterize the **pharmacokinetics** of DIM and to build a pharmacokinetic (**PK**) and pharmacodynamic …

A semi-mechanistic integrated toxicokinetic-toxicodynamic (TK/TD) model for arsenic(III) in hepatocytes.
Stamatelos SK, Androulakis IP, **Kong AN**, Georgopoulos PG. J Theor Biol. 2013 Jan 21;317:244-56. doi: 10.1016/j.jtbi.2012.09.019. Epub 2012 Oct 12. PMID: 23069314 Free PMC article.

Pharmacokinetics and pharmacodynamics of phase II drug metabolizing/antioxidant enzymes gene response by anticancer agent sulforaphane in rat lymphocytes.
Wang H, Khor TO, Yang Q, Huang Y, Wu TY, Saw CL, Lin W, Androulakis IP, **Kong AN.** Mol Pharm. 2012 Oct 1;9(10):2819-27. doi: 10.1021/mp300130k. Epub 2012 Sep 11. PMID: 22931102 Free PMC article.
Moderate increases (2-5-fold) over the time zero were seen for HO-1, Nrf2, and NQO1, and significant increases (>5-fold) for GSTT1, GPx1, and Maf. **PK-PD** analyses using GastroPlus and the bootstrap method provided reasonable fitting for the **PK** and **PD** …

A validated HPLC assay for the determination of R-(-)-gossypol in human plasma and its application in clinical pharmacokinetic studies.

Lin H, Gounder MK, Bertino JR, **Kong AN**, DiPaola RS, Stein MN. J Pharm Biomed Anal. 2012 Jul;66:371-5. doi: 10.1016/j.jpba.2012.03.029. Epub 2012 Mar 24. PMID: 22483642 Free PMC article. Clinical Trial.
The method was successfully applied to characterize the **pharmacokinetics** of AT-101 in a Phase I clinical trial. The validated assay is accurate, and sensitive with minimum loss and rapid analysis time and suitable for quantification of gossypol for **pharmacokinetics** …

Development and validation of an LC-MS-MS method for the simultaneous determination of sulforaphane and its metabolites in rat plasma and its application in pharmacokinetic studies.
Wang H, Lin W, Shen G, Khor TO, Nomeir AA, **Kong AN.** J Chromatogr Sci. 2011 Nov-Dec;49(10):801-6. doi: 10.1093/chrsci/49.10.801. PMID: 22080809

A validated bioanalytical HPLC method for pharmacokinetic evaluation of 2-deoxyglucose in human plasma.
Gounder MK, Lin H, Stein M, Goodin S, Bertino JR, **Kong AN**, DiPaola RS. Biomed Chromatogr. 2012 May;26(5):650-4. doi: 10.1002/bmc.1710. Epub 2011 Sep 19. PMID: 21932382 Free PMC article.
2-Deoxyglucose (2-DG), an analog of glucose, is widely used to interfere with glycolysis in tumor cells and studied as a therapeutic approach in clinical trials. To evaluate the **pharmacokinetics** of 2-DG, we describe the development and validation of a sensitive HPLC fluore …

Pharmacokinetics of dietary cancer chemopreventive compound dibenzoylmethane in rats and the impact of nanoemulsion and genetic knockout of Nrf2 on its disposition.
Lin W, Hong JL, Shen G, Wu RT, Wang Y, Huang MT, Newmark HL, Huang Q, Khor TO, Heimbach T, **Kong AN.** Biopharm Drug Dispos. 2011 Mar;32(2):65-75. doi: 10.1002/bdd.734. Epub 2010 Dec 16. PMID: 21341276 Free PMC article.
An oil-in-water nanoemulsion containing DBM was formulated to potentially overcome the low F* due to poor water solubility of DBM, with enhanced oral absorption. Finally, to examine the role of Nrf2 on the **pharmacokinetics** of DBM, since DBM activates the Nrf2-dependent det …

Metabolism, oral bioavailability and **pharmacokinetics** of chemopreventive kaempferol in rats.
Barve A, Chen C, Hebbar V, Desiderio J, Saw CL, **Kong AN.** Biopharm Drug Dispos. 2009 Oct;30(7):356-65. doi: 10.1002/bdd.677. PMID: 19722166 Free PMC article.

Pharmacokinetics and pharmacodynamics of broccoli sprouts on the suppression of prostate cancer in transgenic adenocarcinoma of mouse prostate (TRAMP) mice: implication of induction of Nrf2, HO-1 and apoptosis and the suppression of Akt-dependent kinase pathway.
Keum YS, Khor TO, Lin W, Shen G, Kwon KH, Barve A, Li W, **Kong AN.** Pharm Res. 2009 Oct;26(10):2324-31. doi: 10.1007/s11095-009-9948-5. Epub 2009 Aug 8. PMID: 19669099
PURPOSE: In the present study, we have evaluated the **pharmacokinetics** and the in vivo prostate chemopreventive activity of broccoli sprouts. ...

Liquid microjunction surface sampling probe electrospray mass spectrometry for detection of drugs and metabolites in thin tissue sections.
Van Berkel GJ, Kertesz V, Koeplinger KA, Vavrek M, **Kong AN.** J Mass Spectrom. 2008 Apr;43(4):500-8. doi: 10.1002/jms.1340. PMID: 18035855

Development and validation of an HPLC method for the determination of dibenzoylmethane in rat plasma and its application to the pharmacokinetic study.
Shen G, Hong JL, **Kong AN.** J Chromatogr B Analyt Technol Biomed Life Sci. 2007 Jun 1;852(1-2):56-61. doi: 10.1016/j.jchromb.2006.12.042. Epub 2007 Jan 10. PMID: 17236826
The utility of the assay was confirmed by the successful analysis of plasma samples from DBM **pharmacokinetics** studies in the rats after oral and intravenous administrations....

In vivo **pharmacokinetics**, activation of MAPK signaling and induction of phase II/III drug metabolizing enzymes/transporters by cancer chemopreventive compound BHA in the mice.

Hu R, Shen G, Yerramilli UR, Lin W, Xu C, Nair S, **Kong AN.** Arch Pharm Res. 2006 Oct;29(10):911-20. doi: 10.1007/BF02973914. PMID: 17121188
Understanding the molecular basis underlying these diverse biological actions of BHA is thus of great importance. Here we studied the **pharmacokinetics**, activation of signaling kinases and induction of phase II/III drug metabolizing enzymes/transporter gene expression by BH …

In vivo **pharmacokinetics** and regulation of gene expression profiles by isothiocyanate sulforaphane in the rat.
Hu R, Hebbar V, Kim BR, Chen C, Winnik B, Buckley B, Soteropoulos P, Tolias P, Hart RP, **Kong AN.** J Pharmacol Exp Ther. 2004 Jul;310(1):263-71. doi: 10.1124/jpet.103.064261. Epub 2004 Feb 26. PMID: 14988420
In this study, we used 4967 oligonucleotides microarray to assess the genes that are modulated by SUL in in vivo rat livers, as well as time course of expression of these genes. The **pharmacokinetics** of SUL was assessed after oral dose of 50 micromol of SUL. ...

Losartan does not affect the **pharmacokinetics** and pharmacodynamics of warfarin.
Kong AN, Tomasko L, Waldman SA, Osborne B, Deutsch PJ, Goldberg MR, Bjornsson TD. J Clin Pharmacol. 1995 Oct;35(10):1008-15. doi: 10.1002/j.1552-4604.1995.tb04018.x. PMID: 8568008 Clinical Trial.
Multiple plasma samples were collected over a 6-day period after both warfarin doses for the measurements of R- and S-warfarin concentrations and prothrombin times. The **pharmacokinetics** of R- and S-warfarin were comparable in the absence and presence of losartan (no signif …

Pharmacokinetics of methylprednisolone hemisuccinate and methylprednisolone in chronic liver disease.
Ludwig EA, **Kong AN**, Camara DS, Jusko WJ. J Clin Pharmacol. 1993 Sep;33(9):805-10. doi: 10.1002/j.1552-4604.1993.tb01955.x. PMID: 8227476
However, good availability of MP from MPHS and lack of perturbation of MP **pharmacokinetics** in CLD patients may provide therapeutic advantages in selection of this glucocorticoid. ...

Disposition of methylprednisolone and its sodium succinate prodrug in vivo and in perfused liver of rats: nonlinear and sequential first-pass elimination.
Kong AN, Jusko WJ. J Pharm Sci. 1991 May;80(5):409-15. doi: 10.1002/jps.2600800502. PMID: 1880717

Pharmacokinetics of methylprednisolone sodium succinate and methylprednisolone in patients undergoing cardiopulmonary bypass.
Kong AN, Jungbluth GL, Pasko MT, Beam TR, Jusko WJ. Pharmacotherapy. 1990;10(1):29-34. PMID: 2179900
The **pharmacokinetics** of methylprednisolone sodium succinate (MPHS) and methylprednisolone (MP) were determined in six patients undergoing open heart surgery with cardiopulmonary bypass. ...

Pharmacokinetics and pharmacodynamic modeling of direct suppression effects of methylprednisolone on serum cortisol and blood histamine in human subjects.
Kong AN, Ludwig EA, Slaughter RL, DiStefano PM, DeMasi J, Middleton E Jr, Jusko WJ. Clin Pharmacol Ther. 1989 Dec;46(6):616-28. doi: 10.1038/clpt.1989.196. PMID: 2689044 Free PMC article.

Simultaneous analysis of methylprednisolone hemisuccinate, cortisol and methylprednisolone by normal-phase high-performance liquid chromatography in human plasma.
Kong AN, Slaughter RL, Jusko WJ. J Chromatogr. 1988 Nov 18;432:308-14. doi: 10.1016/s0378-4347(00)80658-1. PMID: 3065346 No abstract available.

Definitions and applications of mean transit and residence times in reference to the two-compartment mammillary plasma clearance model.
Kong AN, Jusko WJ. J Pharm Sci. 1988 Feb;77(2):157-65. doi: 10.1002/jps.2600770213. PMID: 3361431