Explore the effects of Sulforaphane on the Gut Barrier

Dr Shania Seeber

Co-Founder and Clinical lead of Kenko Health

KBMO DIAGNOSTICS

Dr Shania Seeber

- Co-founder and clinical lead of Kenko Health
- Doctor of Complementary & Alternative Medicine
- Private practice – Radiant Balance
- Author and International speaker
- Passionate about Functional tests and Nutraceutical medicines

Kenko Health

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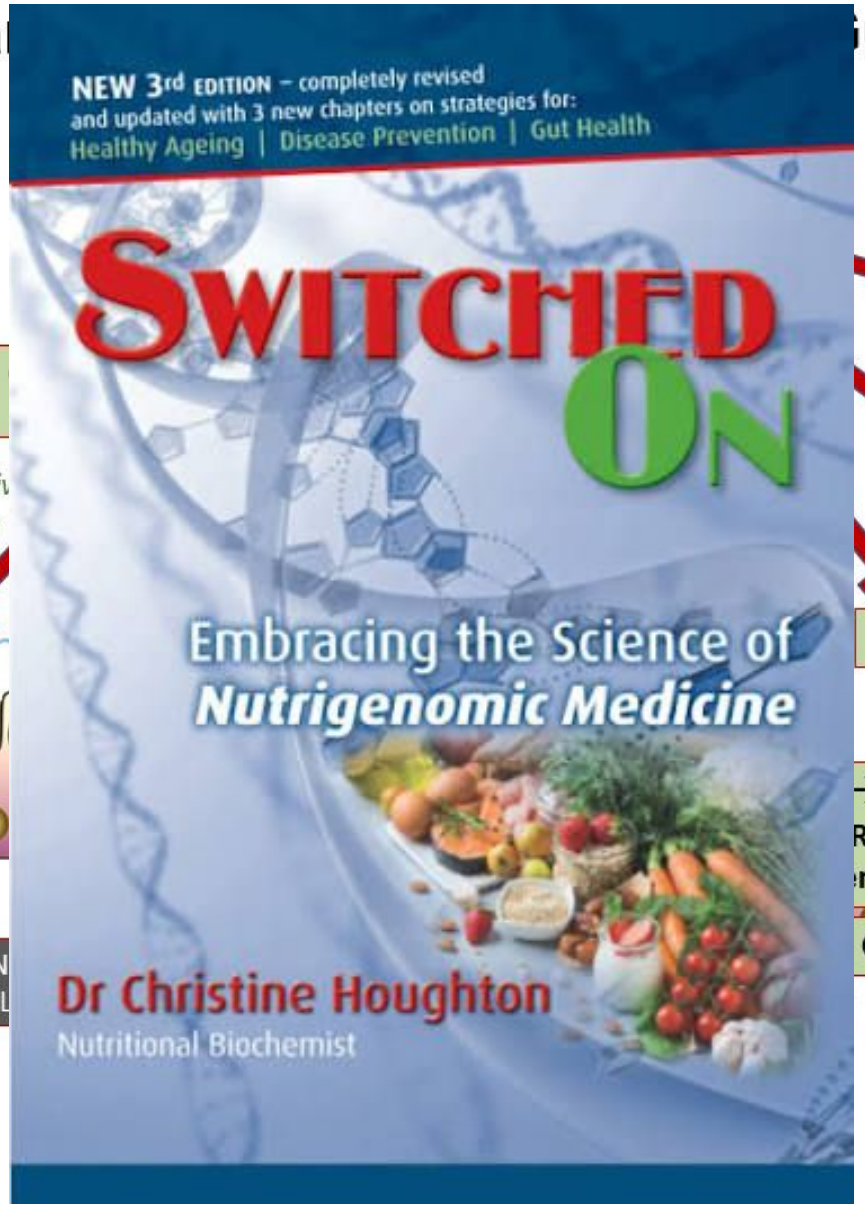
Sulforapha[ane] [Gut] Ecosystem



- INHIBITS UREASE-POSITIVE MICROBES *incl. H.pylori, Klebsiella spp., Pseudomonas spp., Proteus mirabilis, Morganella morganii, Mycobacterium spp.*
- SFN inhibits QUORUM SENSING
- SFN → ↓INFLAMMATION via ↓ Nf-kB

eg. Gram-negativ
Pseudomonas

LPS
TLR4
Gut Lumen
Epithelial Cells
Immune Cells of the Lamina propria
SFN
(INFL

→↑GUT
RIER and Cellular
nces
Gastroparesis

Houghton, C.A. ***The Rationale for Sulforaphane Favourably Influencing Gut Homeostasis and Gut–Organ Dysfunction: A Clinician's Hypothesis***. Int. J. Mol. Sci. **2023**, *24*, 13448.

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BAD STUFF OUT +
GOOD STUFF IN =

HEALTH

YOUR FORMULA TO BEING HEALTHY IN THE MODERN WORLD

DR. SHANIA SEEBER

HARMONIOUS HORMONES =

HEALTH

UNLOCK THE SYMPHONY WITHIN YOUR BODY

DR. SHANIA SEEBER

https://books.by/dr-shania

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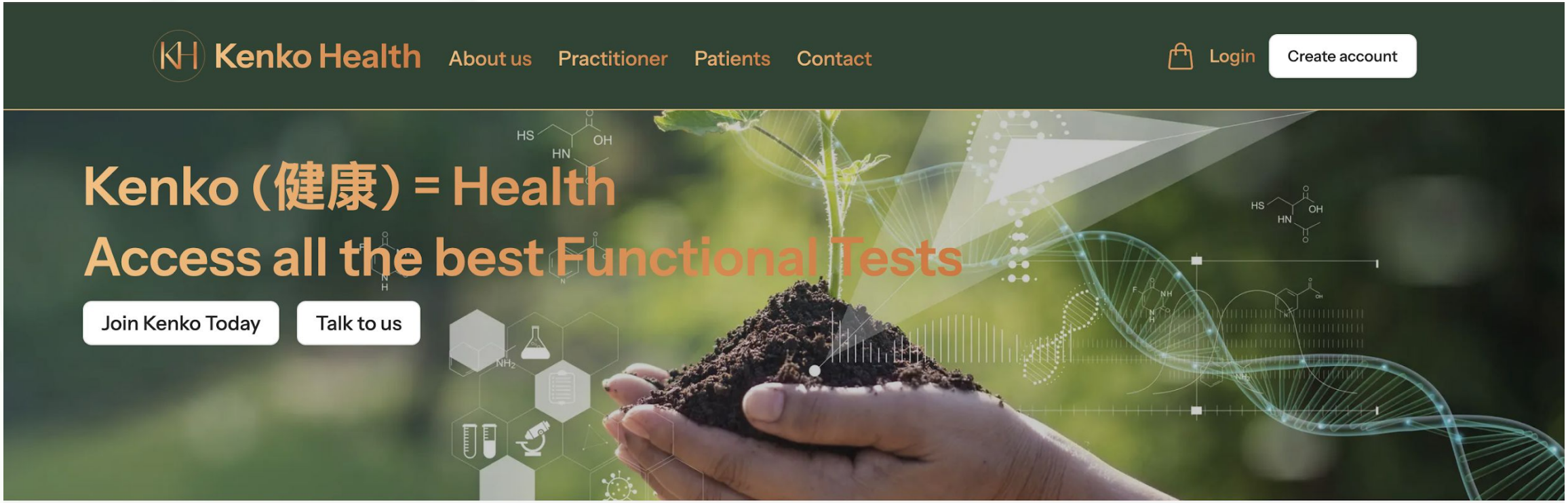

Order, track & get results from multiple lab companies in one place

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Overview

- Nutrigenomics as a tool in your toolbox
- The power in “signaling molecules”
- Sulforaphane as a powerhouse
- NRF2 upregulation and why it is vital
- Gram (-) bacteria, LPS and the Gut Barrier
- Gut Barrier and Sulforaphane

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SULFORAPHANE

*Supports**

- Immune Health*
- Cellular Health*
- Liver Detox*
- Digestion*
- Cognition*

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Nutrigenomic medicine adds to the clinician's toolbox

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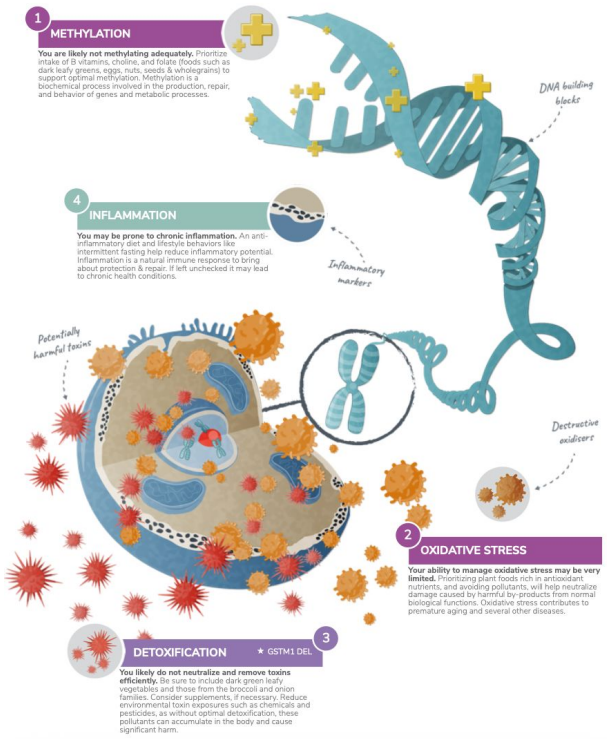
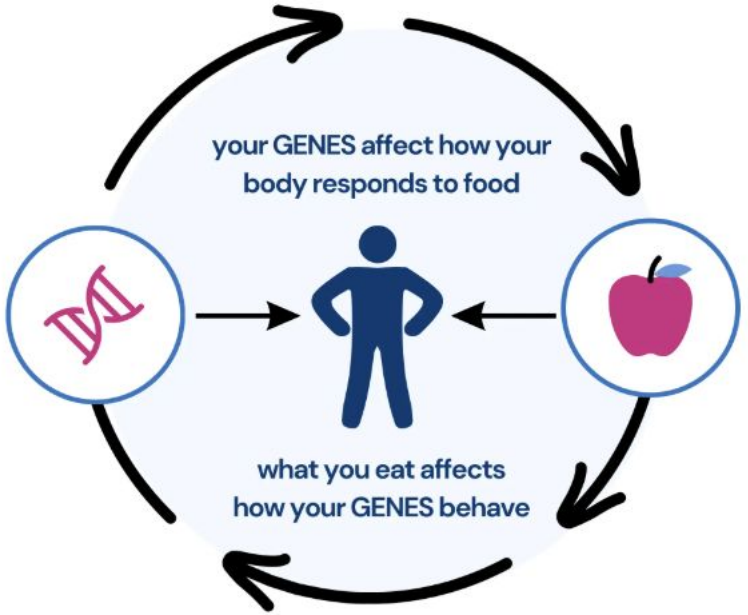
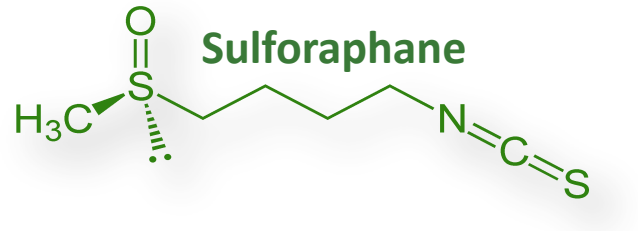
DIAGNOSTICS

What exactly is Nutrigenomics?

NUTRIGENETICS – Identifies gene variants







NUTRIGENOMICS – Identifies food molecules that impact function of gene variants

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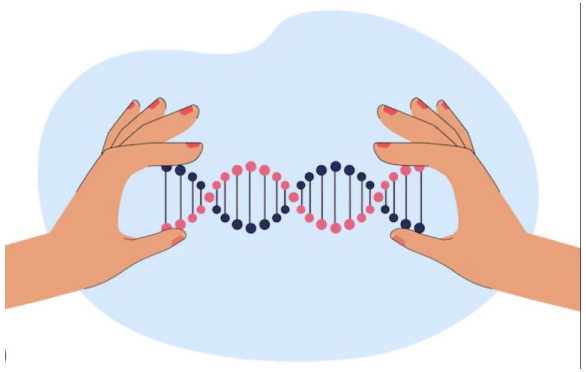
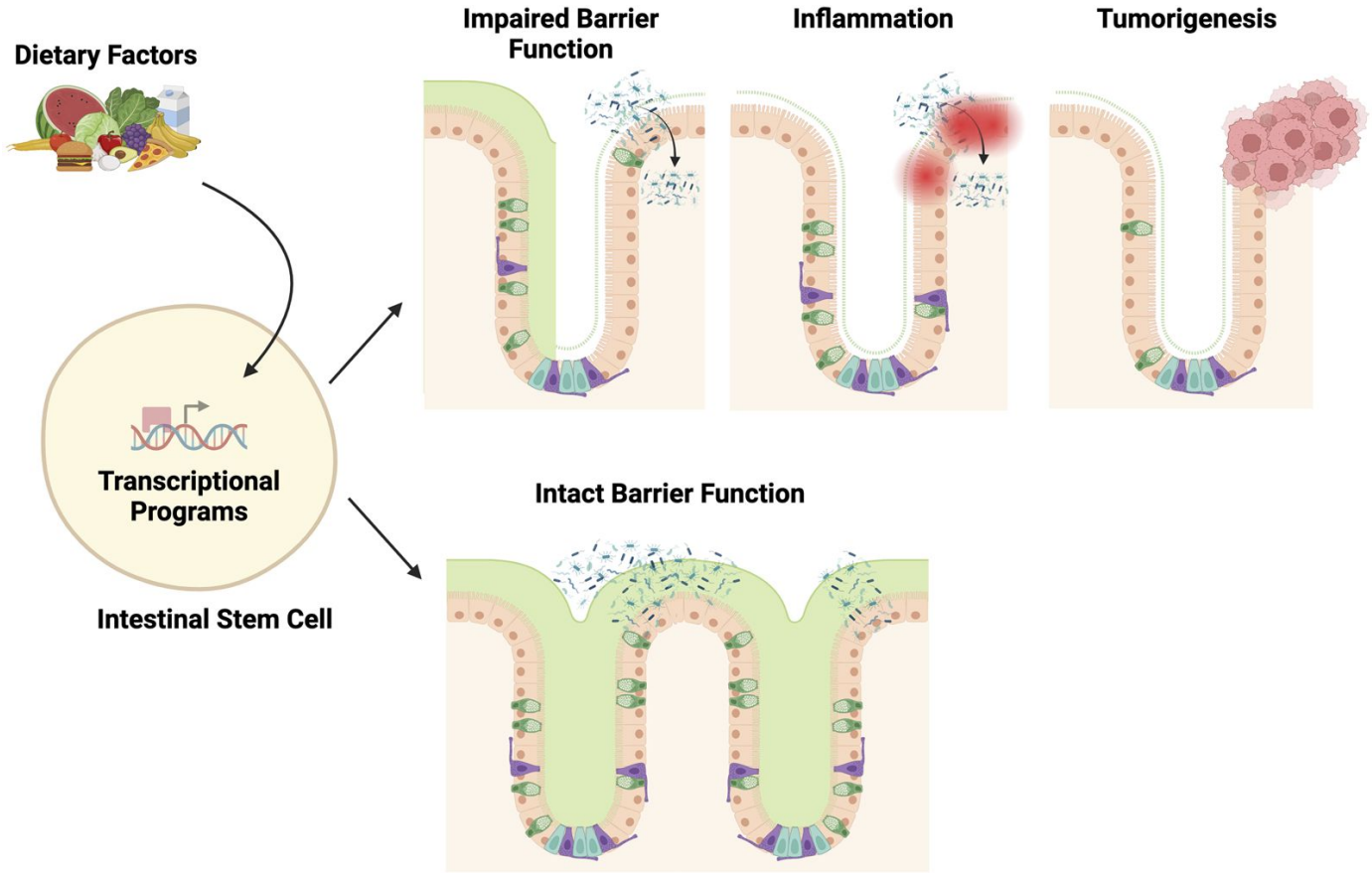
‘Nutrigenomics’ is driving the *paradigm shift* in the practice of Clinical Nutrition



Adding a whole new dimension to ‘personalised medicine’



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The power in “signalling molecules”

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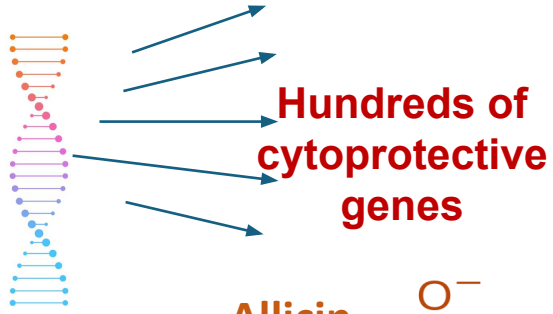
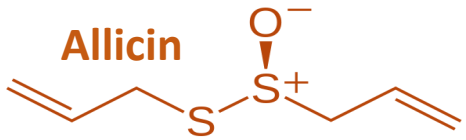
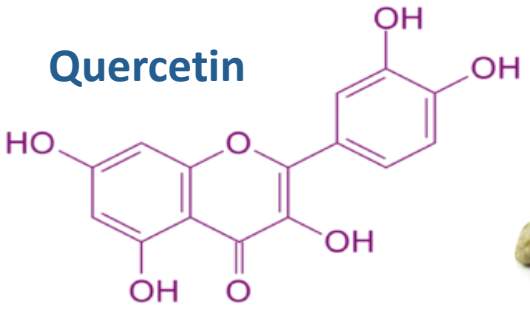
The power of food lies in its signalling molecules

Activation of 100's of protective genes!







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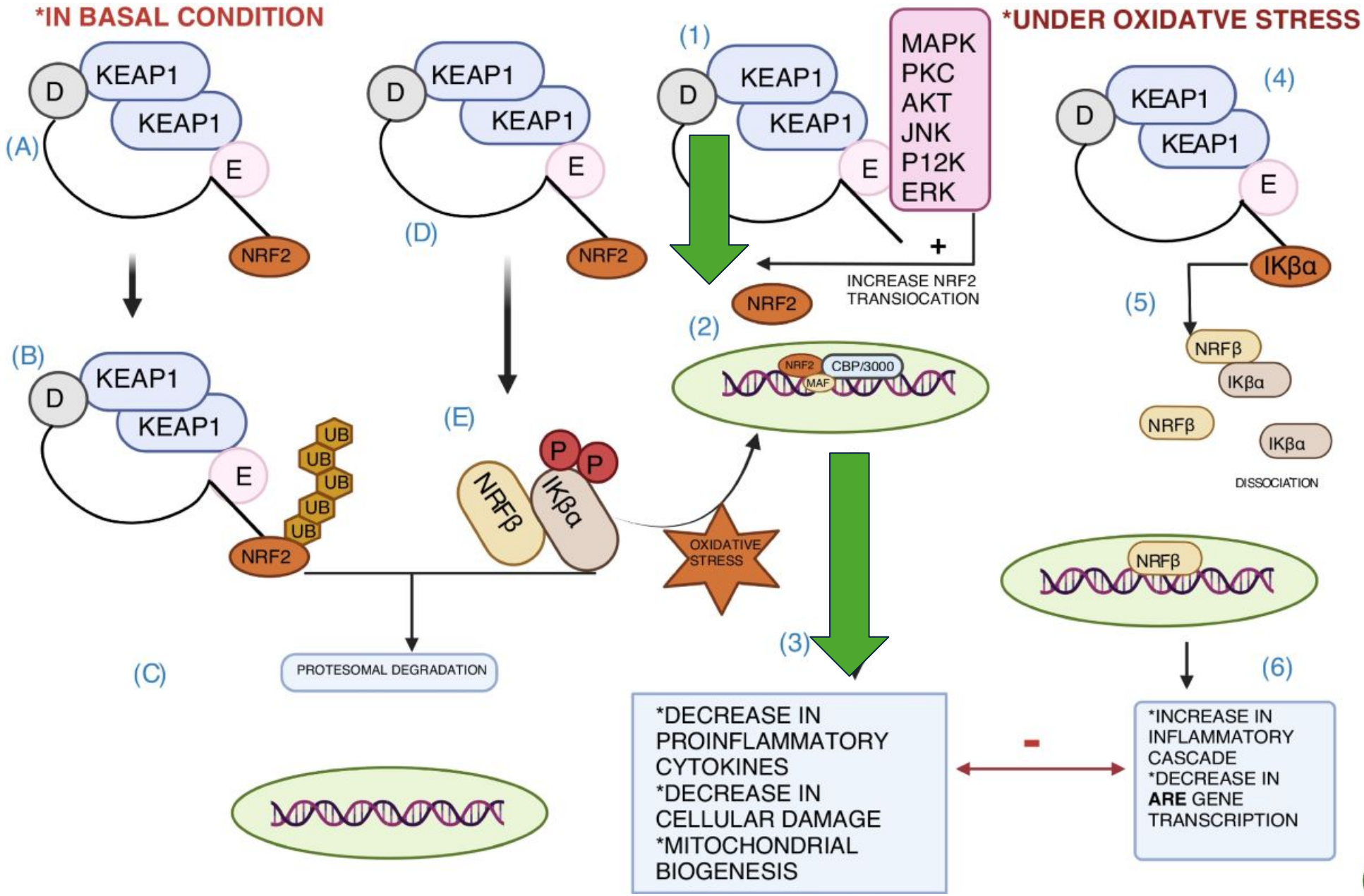

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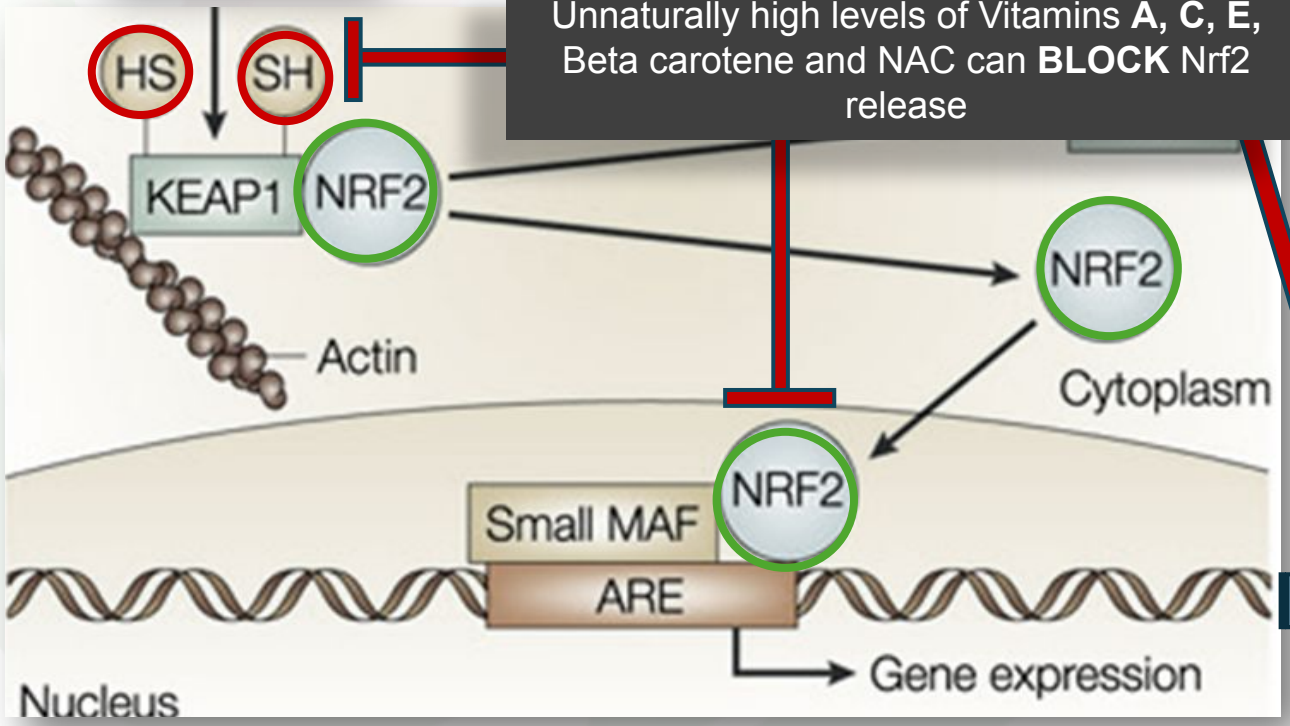
When stressors activate the Nrf2 switch

Broccoli-derived Sulforaphane is a *weak pro-oxidant and* the most potent known natural activator of Nrf2.

Unnaturally high levels of Vitamins **A, C, E,** Beta carotene and NAC can **BLOCK** Nrf2 release



Antioxidant Defences

Modulates Inflammation

Detox

Energy (ATP)

Nrf2 activates 100's of protective genes

T. W. Kensler, G.-S. Qian, J.-G. Chen, and J. D. Groopman, *"Translational strategies for cancer prevention in liver,"* Nature Reviews Cancer, vol. 3, no. 5, pp. 321–329, 2003

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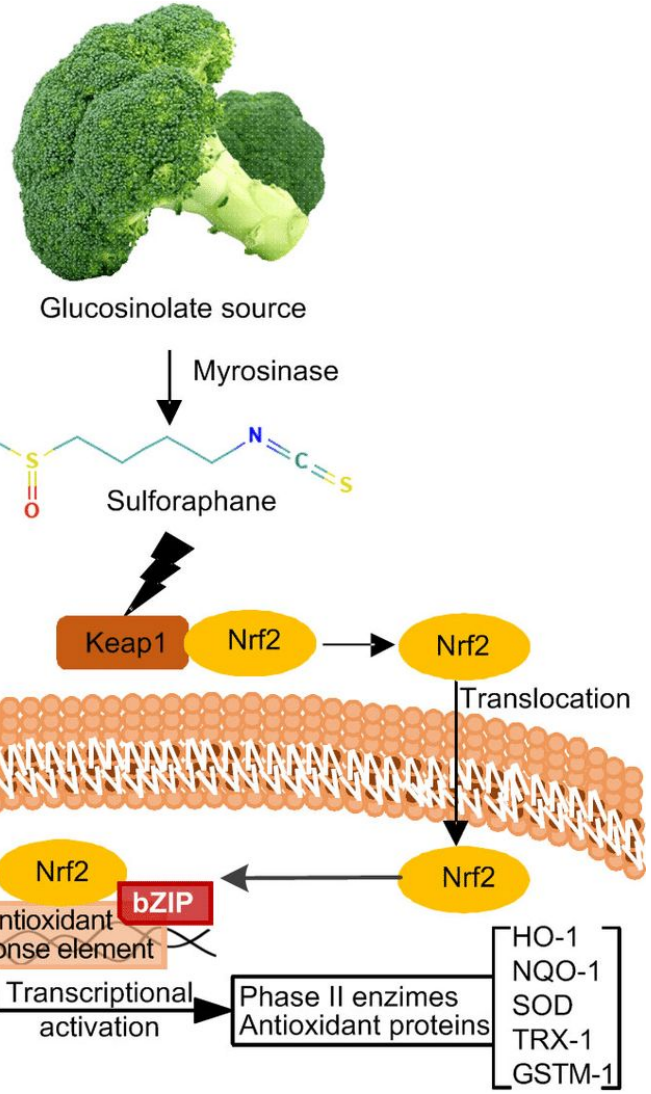
Sulforaphane & nutrigenomic activity

Sulforaphane

Sulforaphane is the most potent naturally-occurring Nrf2 activator



Activates antioxidant and detox genes and inhibits NF-kB

https://www.researchgate.net/figure/Effect-of-SFN-on-the-transcription-factor-Nrf2-After-the-reaction-of-the-enzyme_fig1_340511859

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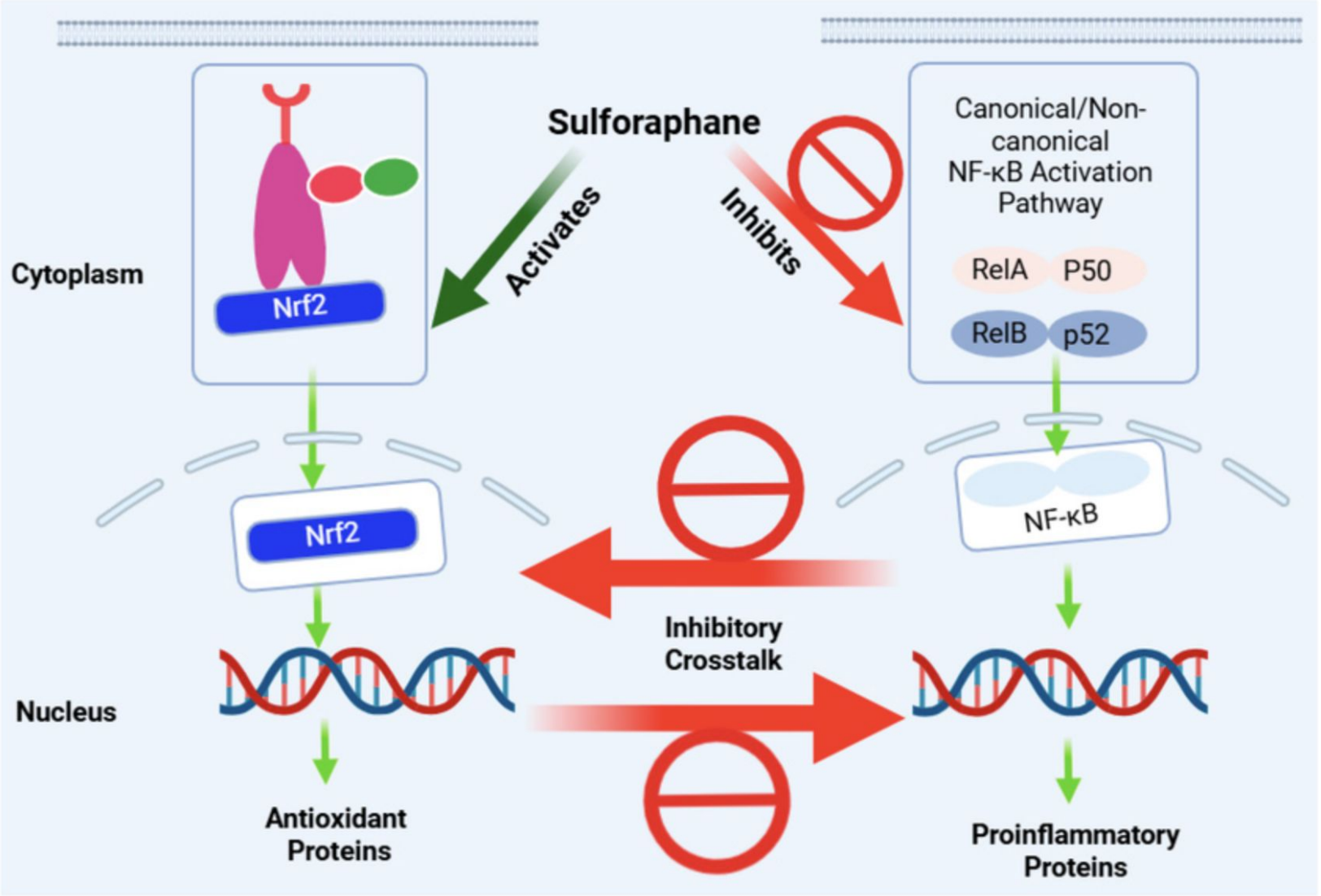
Sulforaphane & NF Kappa B



https://www.researchgate.net/figure/Anti-inflammatory-effect-of-sulforaphane-via-crosstalk-of-the-Nrf2-and-NF-kB-pathways_fig6_380855449

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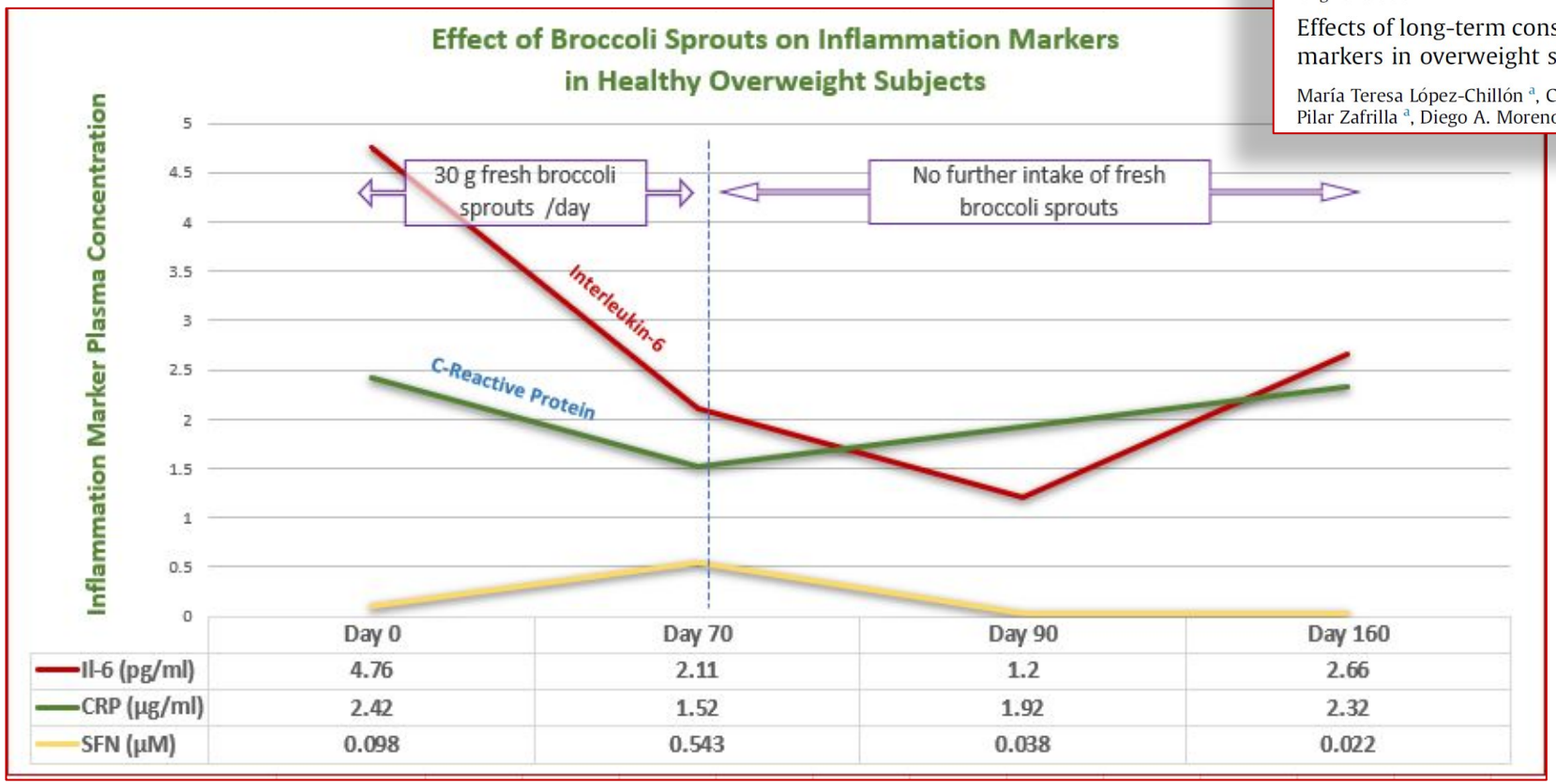
Using signalling molecules →↓ NF-kB



	Day 0	Day 70	Day 90	Day 160
Il-6 (pg/ml)	4.76	2.11	1.2	2.66
CRP (µg/ml)	2.42	1.52	1.92	2.32
SFN (µM)	0.098	0.543	0.038	0.022

Lopez-Chillon MT et al. ***Effects of long-term consumption of broccoli sprouts on inflammatory markers in overweight subjects***. *Clin Nutr. 2018 Mar 13. S0261-5614(18)30118-3.*

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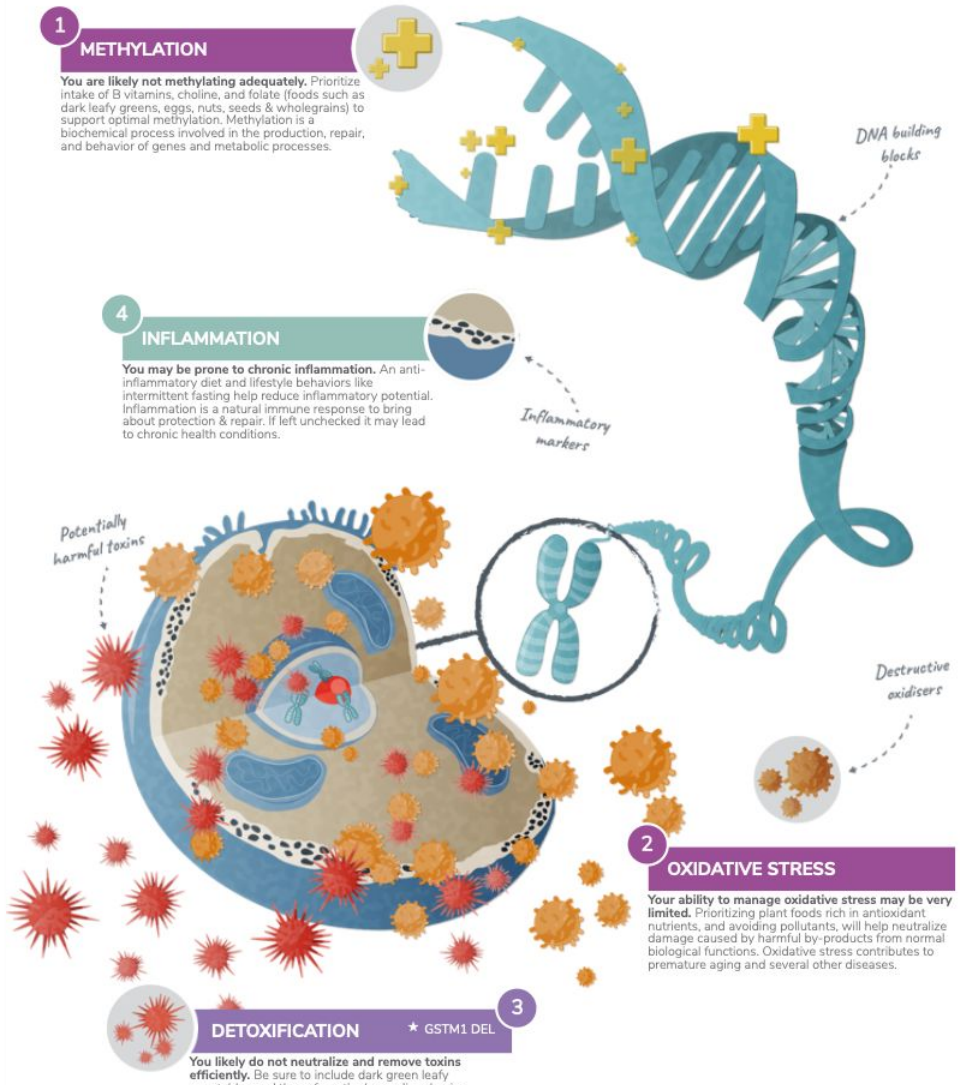
PATHWAY-BASED RESULTS

Hugh Raye

	PATHWAY	IMPACT
CELLULAR	Methylation	VERY HIGH
	Oxidative stress	VERY HIGH
	Detoxification	HIGH
	Inflammation	MEDIUM
SYSTEMS	Glucose & insulin	VERY HIGH
	Memory & brain health	VERY HIGH
	Collagen & joints	HIGH
	Mood & behavior	HIGH
	Bone health	HIGH
	Hormone balance	MEDIUM
	Histamine overload	LOW
CARDIOVASCULAR HEALTH	Vascular health	MEDIUM
	Cholesterol	MEDIUM
	Blood pressure	MEDIUM
	Blood clotting	LOW
ENERGY	Pro-inflammatory fat	VERY HIGH
	Weight gain & weight loss resistance	VERY HIGH
	Adipogenesis	HIGH
	Exercise response	HIGH
	Energy expenditure	HIGH
	Appetite/Satiety/Intake	LOW
ACTIVITY	Injury	VERY HIGH
	Endurance	HIGH
	Recovery	MEDIUM
	Power	LOW
	Training response	LOW
NUTRIENTS	Vitamin B12	VERY HIGH
	Folate	HIGH
	Salt	MEDIUM
	Vitamin D	MEDIUM
	Choline	LOW
	Fatty acids	LOW
	Caffeine	LOW
	Vitamin C	LOW
	Gluten	LOW
	Iron overload	LOW

CELLULAR OVERVIEW

We are the sum of our cells, and we are only as healthy as they are. Every cell in our body functions independently yet is connected to the whole. Like a small apartment inside a high-rise building, each unit takes care of its own day-to-day maintenance, but ultimately contributes to the overall functionality of the building.



METHYLATION 1		OXIDATIVE STRESS 2	
COMT Val158Met G>A	GA	MNSOD Val16Ala T>C	TT
MTHFR 1298 A>C	AC	PPARGC1A Gly482Ser G>A	GA
MTHFR 677 C>T	CT	ENOS Glu298Asp G>T	TT
MTR 2756 A>G	GG	GSTM1 INS/DEL	DEL
TCN2 776 C>G	GG	NQO1 Pro187Ser C>T	CT
CBS 699 C>T	CT	PPARG Pro12Ala C>G	CC
MTHFD1 1958 G>A	GA	GPX1 Pro198Leu C>T	CT
MTRR 66 A>G	AG	HO-1 –413 A>T	AT
NBPF3 T>C	TC	PON1 Gln192Arg A>G	AG
NQO1 Pro187Ser C>T	CT	TNFA –308 G>A	GA
PEMT –744 G>C	GC	CAT –262 C>T	CC
BHMT Arg239Glu G>A	GA	ALDH2 Glu504Lys G>A	GG
OGG1 Ser326Cys C>G	CC	APOE E2/E3/E4	E3/E3
		GSTO2 Asn142Asp A>G	AA

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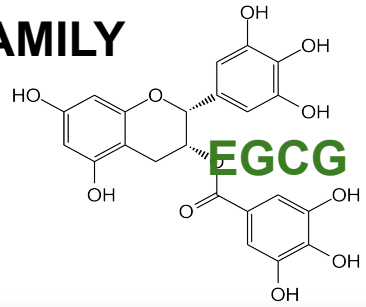
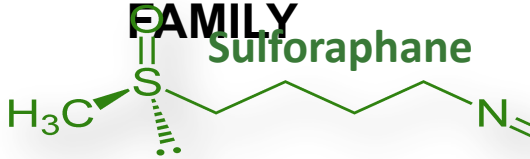
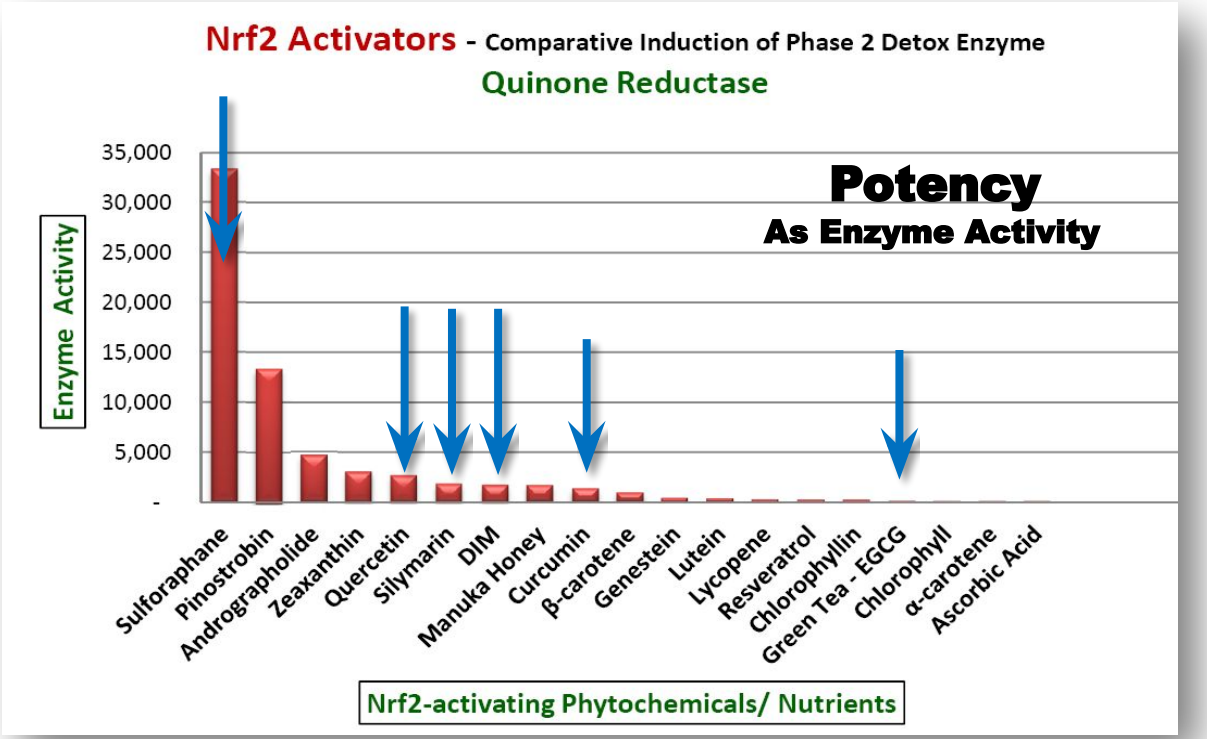
What makes Sulforaphane different?

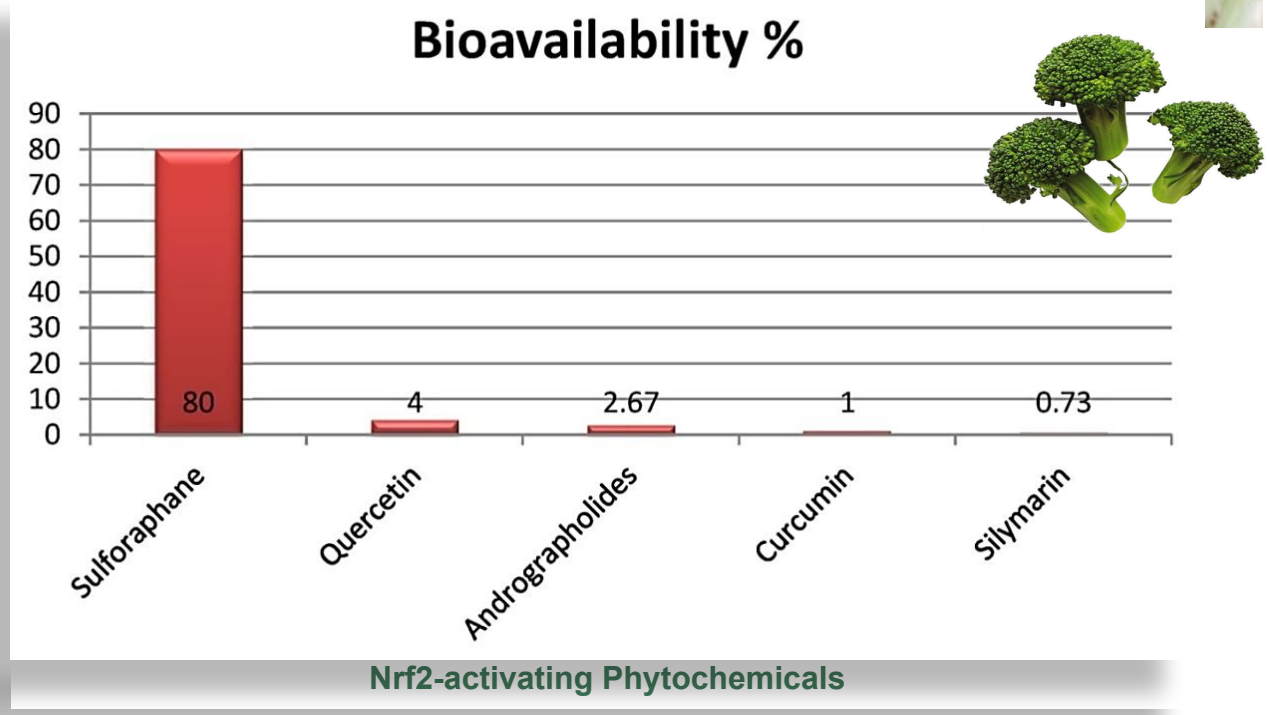
POLYPHENOL FAMILY



ORGANOSULFUR FAMILY







Houghton CA. et al. ***Sulforaphane and Other Nutrigenomic Nrf2 Activators: Can the Clinician's Expectation Be Matched by the Reality?*** *Oxidative Medicine and Cellular Longevity. 2016: Article 7857186 1-17.*

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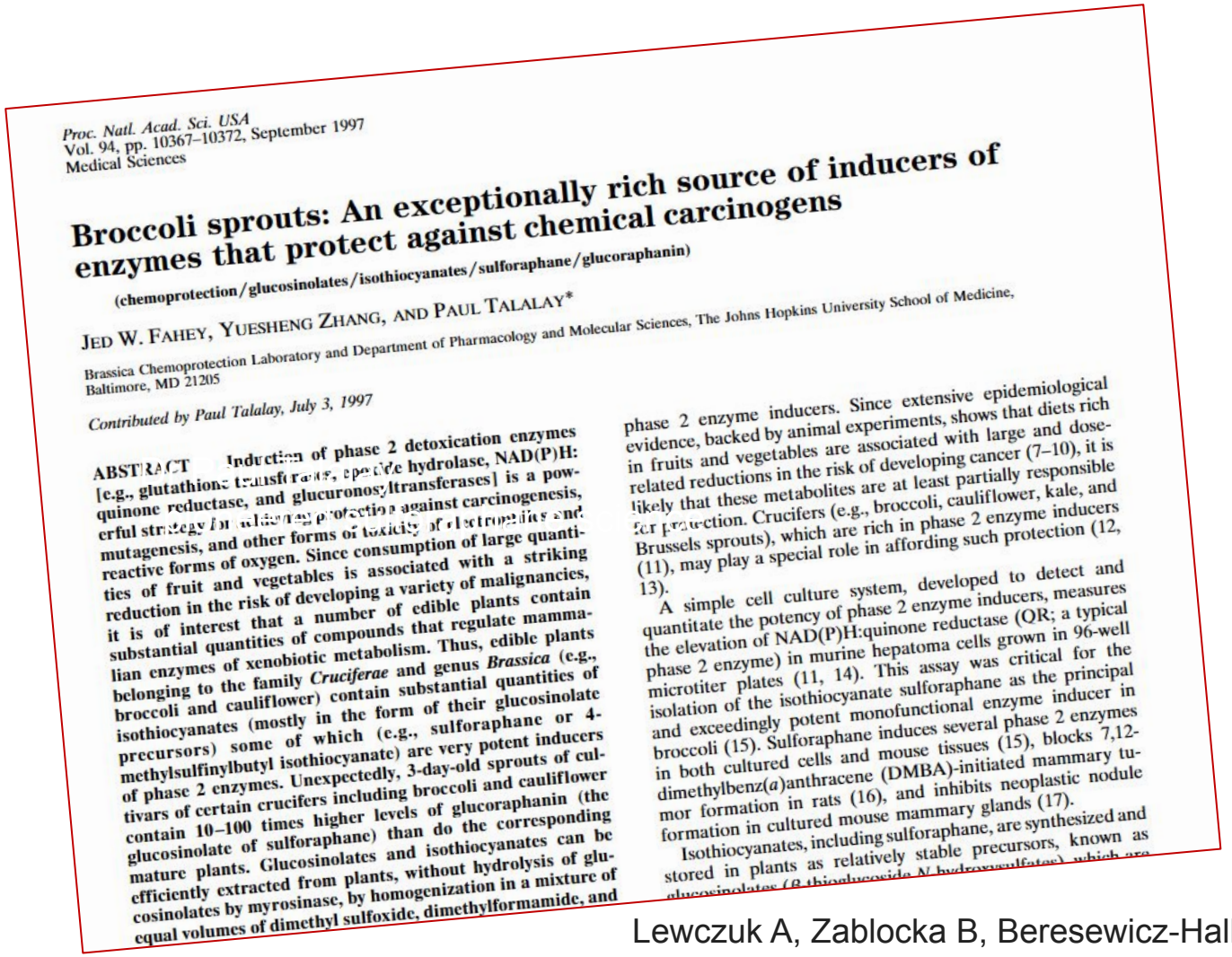
Sulforaphane – key to phase 2 detoxification



Proc. Natl. Acad. Sci. USA
Vol. 94, pp. 10367–10372, September 1997
Medical Sciences

Broccoli sprouts: An exceptionally rich source of inducers of enzymes that protect against chemical carcinogens

(chemoprotection/glucosinolates/isothiocyanates/sulforaphane/glucoraphanin)

JED W. FAHEY, YUESHENG ZHANG, AND PAUL TALALAY*

Brassica Chemoprotection Laboratory and Department of Pharmacology and Molecular Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD 21205

Contributed by Paul Talalay, July 3, 1997

ABSTRACT Induction of phase 2 detoxication enzymes [e.g., glutathione transferase, epoxide hydrolase, NAD(P)H: quinone reductase, and glucuronosyltransferases] is a powerful strategy for achieving protection against carcinogenesis, mutagenesis, and other forms of toxicity of electrophiles and reactive forms of oxygen. Since consumption of large quantities of fruit and vegetables is associated with a striking reduction in the risk of developing a variety of malignancies, it is of interest that a number of edible plants contain substantial quantities of compounds that regulate mammalian enzymes of xenobiotic metabolism. Thus, edible plants belonging to the family *Cruciferae* and genus *Brassica* (e.g., broccoli and cauliflower) contain substantial quantities of isothiocyanates (mostly in the form of their glucosinolate precursors) some of which (e.g., sulforaphane or 4-methylsulfinylbutyl isothiocyanate) are very potent inducers of phase 2 enzymes. Unexpectedly, 3-day-old sprouts of cultivars of certain crucifers including broccoli and cauliflower contain 10–100 times higher levels of glucoraphanin (the glucosinolate of sulforaphane) than do the corresponding mature plants. Glucosinolates and isothiocyanates can be efficiently extracted from plants, without hydrolysis of glucosinolates by myrosinase, by homogenization in a mixture of equal volumes of dimethyl sulfoxide, dimethylformamide, and

phase 2 enzyme inducers. Since extensive epidemiological evidence, backed by animal experiments, shows that diets rich in fruits and vegetables are associated with large and dose-related reductions in the risk of developing cancer (7–10), it is likely that these metabolites are at least partially responsible for protection. Crucifers (e.g., broccoli, cauliflower, kale, and Brussels sprouts), which are rich in phase 2 enzyme inducers (11), may play a special role in affording such protection (12, 13).

A simple cell culture system, developed to detect and quantitate the potency of phase 2 enzyme inducers, measures the elevation of NAD(P)H:quinone reductase (QR; a typical phase 2 enzyme) in murine hepatoma cells grown in 96-well microtiter plates (11, 14). This assay was critical for the isolation of the isothiocyanate sulforaphane as the principal and exceedingly potent monofunctional enzyme inducer in broccoli (15). Sulforaphane induces several phase 2 enzymes in both cultured cells and mouse tissues (15), blocks 7,12-dimethylbenz(*a*)anthracene (DMBA)-initiated mammary tumor formation in rats (16), and inhibits neoplastic nodule formation in cultured mouse mammary glands (17).

Isothiocyanates, including sulforaphane, are synthesized and stored in plants as relatively stable precursors, known as

Nrf2 Target Genes include:

METHYLATION	1	OXIDATIVE STRESS	2	DETOXIFICATION	3	INFLAMMATION	4
COMT Val158Met G>A				GSTM1 INS/DEL	DEL	IL-1 +/–	+
MTHFR 1298 A>C			A	CYP1B1 Leu432Val C>G	GG	CRP 2147 G>A	GG
MTHFR 677 C>T	CT	Gly482Ser G>A		NAT2 R/I/S	Slow	ENOS Glu298Asp G>T	TT
MTR 2756 A>G	GG	ENOS Glu298Asp G>T	TT	COMT Val158Met G>A	GA	CYP1B1 Leu432Val C>G	GG
TCN2 776 C>G		GSTM1 INS/DEL	DEL	MNSOD Val16Ala T>C	TT	HNMT Thr105Ile C>T	CT
CBS 699 C>T				NQO1 Pro187Ser C>T	CT	MNSOD Val16Ala T>C	TT
MTHFD1 1958 G>A				CYP17A1 34 T>C	TC	SIRT1 994 T>C	TT
MTRR 66 A>G	AG	HO-1 –413 A>T	AT	CYP2C9 Arg144Cys C>T	CT	FADS1 592 G>T	GT
NBPF3 T>C	TC	PON1 Gln192Arg A>G	AG	MTHFR 677 C>T	CT	HO-1 –413 A>T	AT
NQO1 Pro187Ser C>T	CT	TNFA –308 G>A	GA	PON1 Gln192Arg A>G	AG	IL-6R Asp358Ala A>C	AC
PEMT –744 G>C	GC	CAT –262 C>T	CC	ALDH2 Glu504Lys G>A	GG	TNFA –308 G>A	GA
BHMT Arg239Glu G>A	GA	ALDH2 Glu504Lys G>A	GG	CYP1A1 Ile462Val A>G	AA	APOE E2/E3/E4	E3/E3
OGG1 Ser326Cys C>G	CC	APOE E2/E3/E4	E3/E3	CYP1A2 –163 A>C	AA	CYP1A1 Ile462Val A>G	AA
		GSTO2 Asn142Asp A>G	AA	CYP1B1 Asn453Ser A>G	AA	DAO His645Asp C>G	CC
		GSTP1 Ile105Val A>G	AA	CYP2C19 *1/*2/*17	*1/*1	FOXO3 G>T	GT
		GSTT1 INS/DEL	INS	CYP2C9 Ile359Leu A>C	AA	FUT2 Trp153Ter G>A	GA
		HFE C282Y/H63D	CC/HH	CYP2D6 *1/*3/*10	*1/*1	HLA DQ 2.2/2.5/8	DQ2.2/DQ2.2
		OGG1 Ser326Cys C>G	CC	CYP3A4 –392 A>G	AA	IL-6 –174 G>C	GG
		UCP1 –3826 A>G	AA	EPHX1 Tyr113His T>C	TT	PPARA 89204 G>C	GG
		UCP2 –866 G>A	GG	GSTO2 Asn142Asp A>G	AA	TIMP4 –55 T>C	CT
		UCP3 –55 C>T	CC	GSTP1 Ala114Val C>T	CC	TNFA –238 G>A	GG
				GSTP1 Ile105Val A>G	AA		
				GSTT1 INS/DEL	INS		
				NAT1 Arg187Gln G>A	GG		
				SULT1A1 Arg213His G>A	GG		

Lewczuk A, Zablocka B, Beresewicz-Haller M. ***Is Nrf2 Behind Endogenous Neuroprotection of the Hippocampal CA2-4,DG Region?*** *Mol Neurobiol*. 2023 Mar;60(3):1645-1658.

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The activation of Sulforaphane

Myrosinase Enzyme

Essential for Sulforaphane Formation

Activated by Cutting, Chewing...

Inactive Precursor
GLUCORAPHANIN

Bioactive Compound
SULFORAPHANE

Only 100% Whole Broccoli sprouts contain
ACTIVE myrosinase enzyme

Broccoli Seed Extracts containing *ONLY Glucoraphanin* have NO clinical effect

Nestle M. ***Broccoli sprouts as inducers of carcinogen-detoxifying enzyme systems***: *Proc Nat Acad Sci.* Vol.94, 11149-11151, 1997

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Understanding the Sulforaphane yield

1 **100% whole broccoli sprouts are essential to provide:**

Precursor GLUCORAPHANIN* + Myrosinase → SULFORAPHANE

In its WHOLE food matrix

2 Seed extracts have no Myrosinase

Precursor GLUCORAPHANIN* + ~~Myrosinase~~ → ~~SULFORAPHANE~~

3 Home grown?

Highly Variable Precursor GLUCORAPHANIN* + Variable Myrosinase → ↓↓↓ SULFORAPHANE

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And now let’s focus on the gut…

- Sulforaphane, a compound found in cruciferous vegetables like broccoli, strengthens the gut barrier by increasing tight junction proteins (e.g., ZO-1, Occludin) and reducing intestinal inflammation.
- It acts as a potent antioxidant, activating the Nrf2 pathway to combat oxidative stress and protecting against increased intestinal permeability or "leaky gut".

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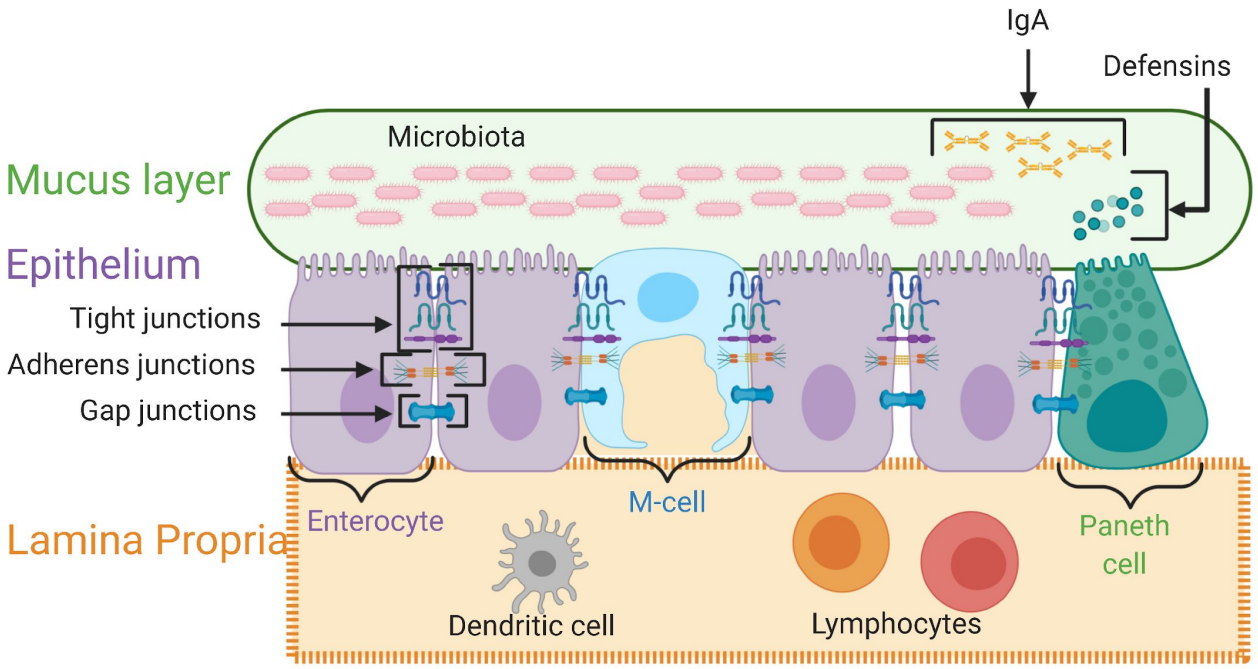
The Intestinal Barrier (IB)



Source: Sharma & Riva, 2022

- The first line of defence against pathogens and food antigens
- In a healthy person, it operates on selective permeability. Water, ions and low-molecular substances can freely pass through. Macromolecules, toxins, food allergens and pathogens cannot.
- When the latter substances permeate the IB, the immune system is over-activated, resulting in a systemic inflammatory response.
- Maintaining the integrity of the intestinal barrier is key for your clients' wellbeing.

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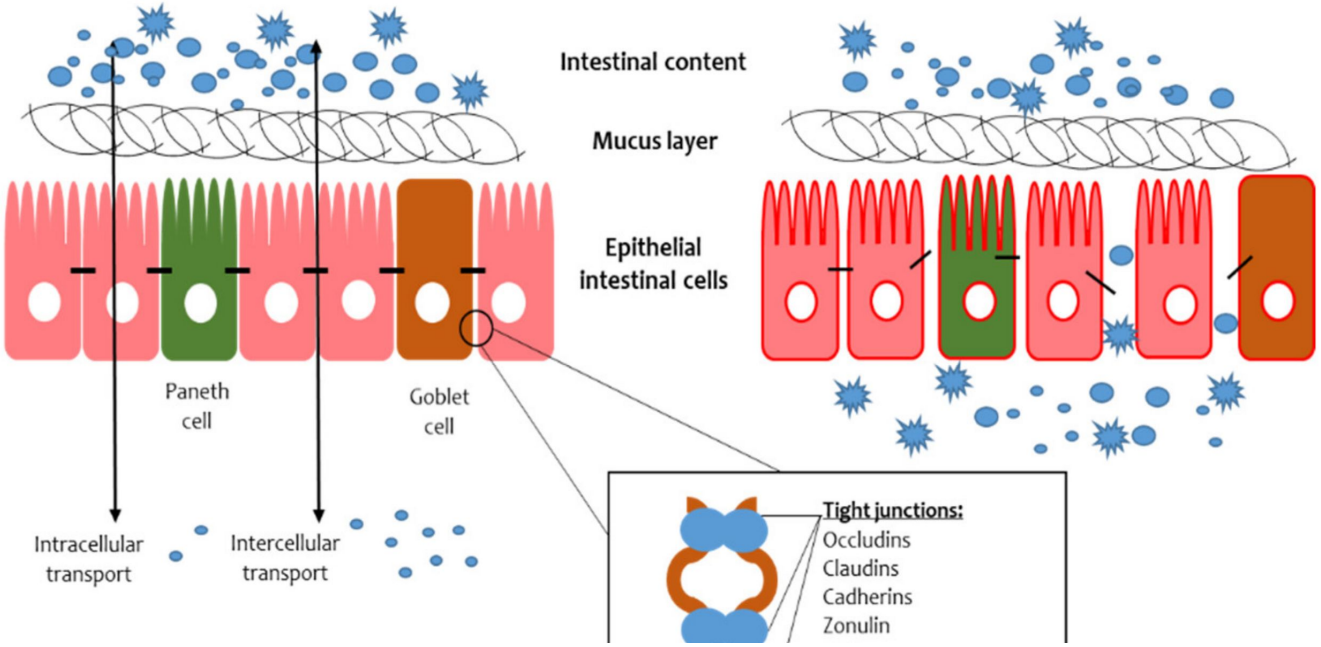
Intestinal Permeability – “Leaky Gut”



Source: Kocot, Jarocka-Cyrta & Drabinska, 2022

- The lining of the small intestine becomes damaged and more porous.
- Allows toxins, bacteria and other particles to “leak” into the bloodstream.
- Contributes to excessive immune reactions.
- Triggers and mediates systemic inflammation.
- Is associated with a wide range of symptoms, including food sensitivities, bloating, fatigue, headaches, joint pain, skin issues and nutritional deficiencies.

Remember: A level of intestinal cell permeability is normal for nutrient absorption!
But “leaky gut” involves compromised epithelial tight junctions.

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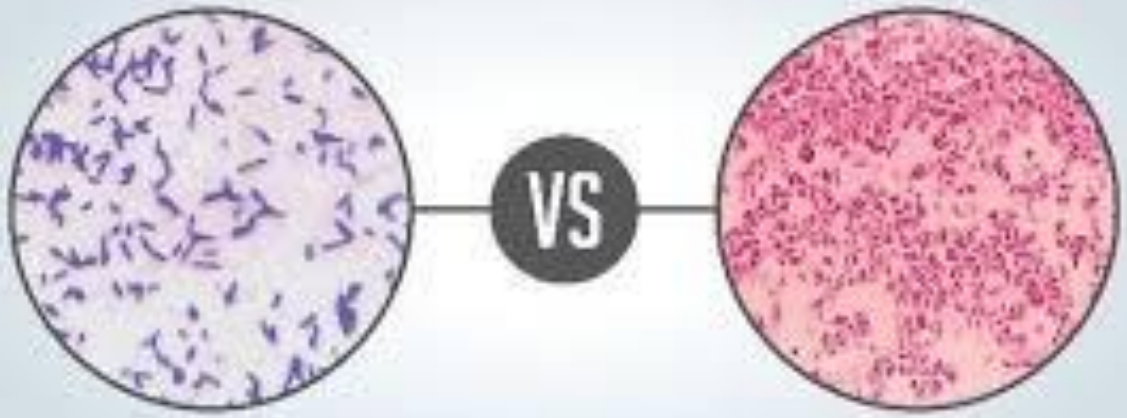
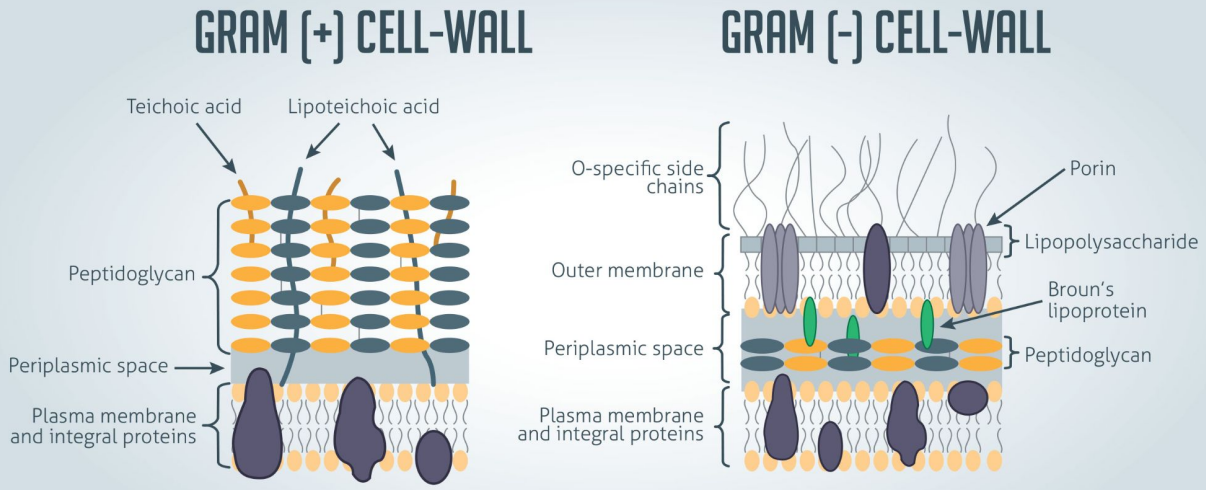
Gram negative bacteria, LPS and gut permeability





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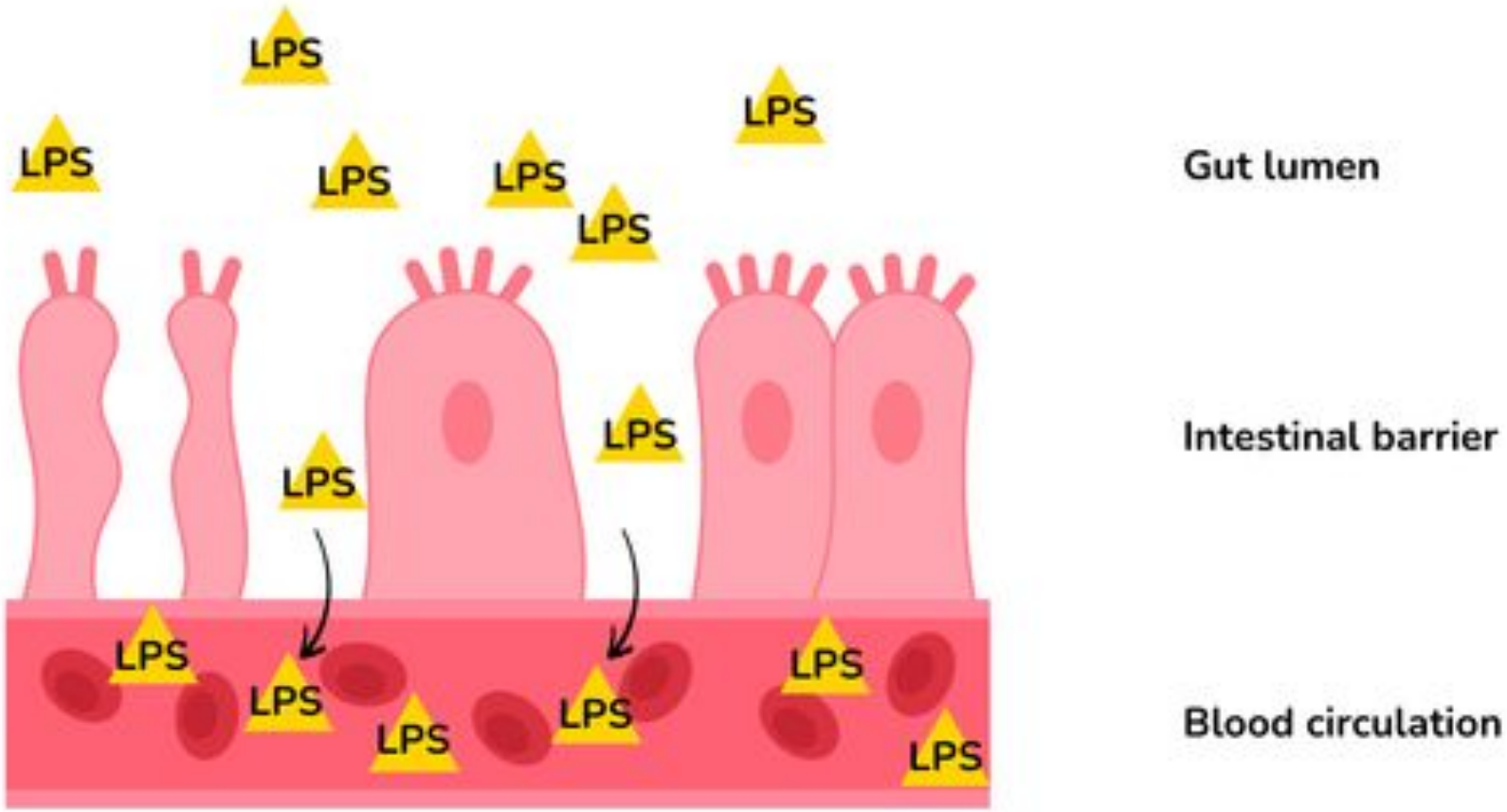

Chronic Inflammation & Immune Activation

Metabolic Syndrome

Neurological Disorders

Liver Disease

https://www.nature.com/articles/s41598-017-06885-7

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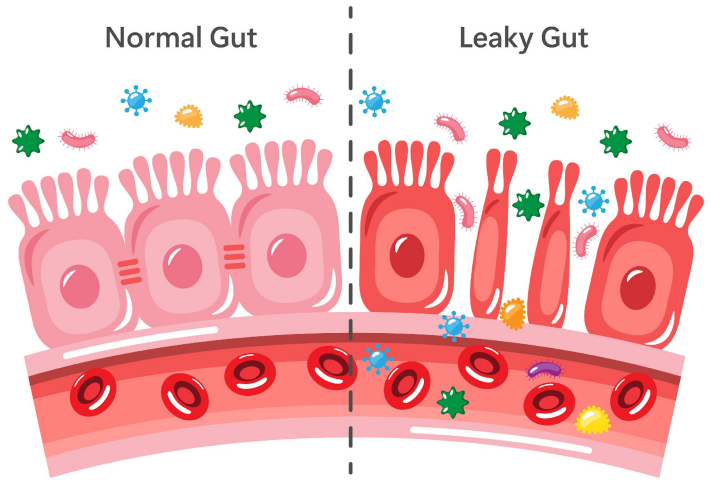
Gut Barrier Panel				
	IgG1-4+C3d		IgA1-2	
		Cut off		Cut off
Candida	Negative		Positive	
Zonulin	Negative		Positive	
Occludin	Negative		Negative	
LPS	Negative		Positive	



KBMO's unique Gut Barrier Panel acknowledges that leaky gut occurs across a spectrum and includes the gatekeeper markers: Candida, Zonulin, Occludin and LPS.

For each marker we measure IgG 1-4 / C3d, in addition to IgA 1-2.

KBMO DIAGNOSTICS

Candida

Naturally occurring yeast, residing in the GI tract as part of the normal microbiome. Overgrowth is problematic.

We measure and use any candida overgrowth in the stomach/dysbiosis as a precursor to leaky gut occurrence

Zonulin

A marker of intestinal permeability. We use unique next generation Zonulin IgG **antibody** screening – a more stable and specific marker, exclusive to KBMO.

Developed by Dr Alessio Fasano & Dr Brent Dorval

Occludin

A marker of intestinal tight junction stabilization and optimal barrier function.

Elevated occludin indicates that the tight junctions between intestinal epithelial cells are breaking down

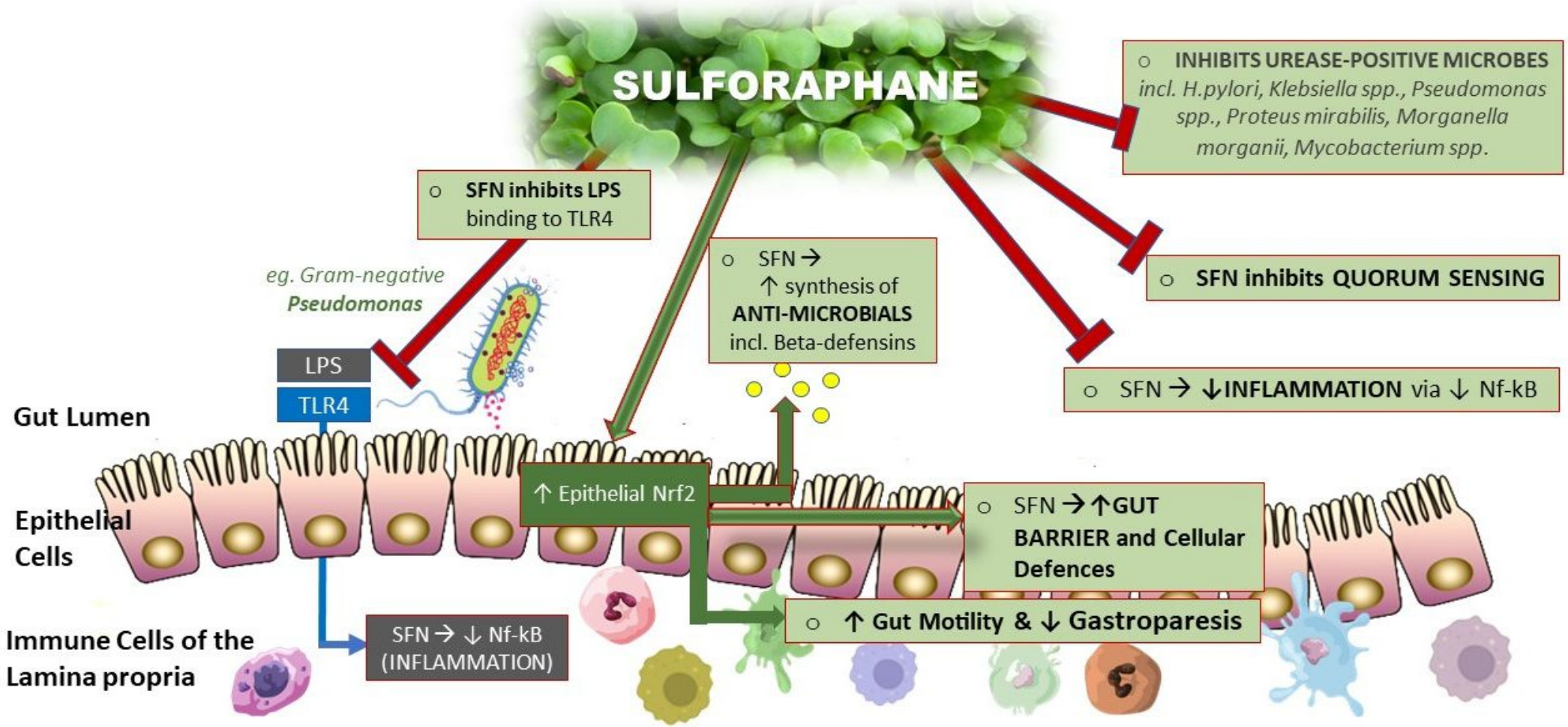
Lipopolysaccharide (LPS)

Potent endotoxin, present in outer surface membrane of gram-negative bacteria - many of which are pathogenic.

Major inducer of inflammatory response - triggers inflammatory cytokine release, can create direct epithelial damage in the gut, crosses the blood brain barrier.

KBMO DIAGNOSTICS

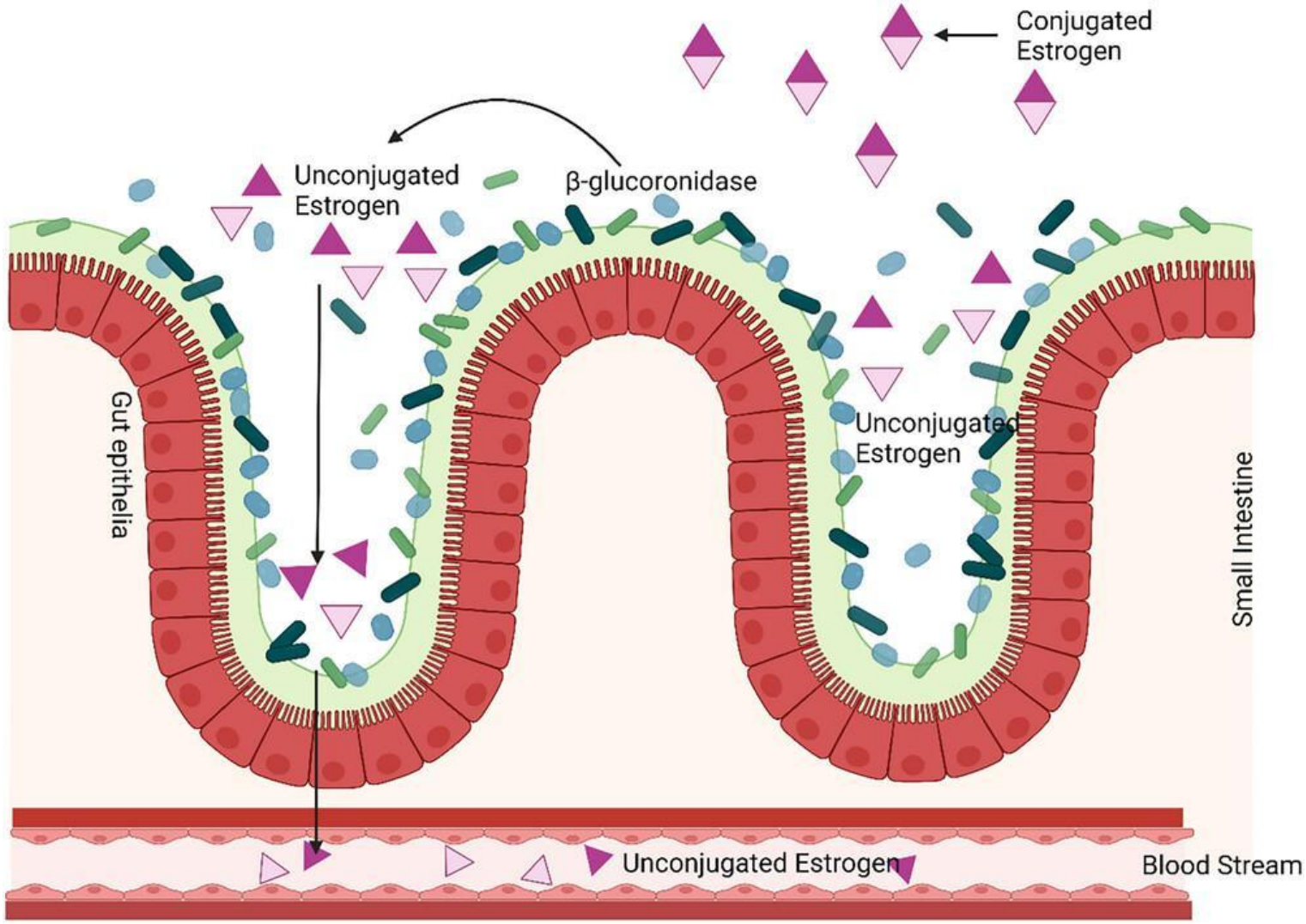
Sulforaphane's Key Effects on the Gut Ecosystem



Houghton, C.A. ***The Rationale for Sulforaphane Favourably Influencing Gut Homeostasis and Gut–Organ Dysfunction: A Clinician's Hypothesis***. *Int. J. Mol. Sci.* **2023**, *24*, 13448.

KBMO DIAGNOSTICS

Gut Barrier, the Estrobolome and Sulforaphane



KBMO
DIAGNOSTICS

TEST NAME	RESULTS | 07/26/18	RANGE
Urinary Estrogens		
Estradiol	0.68 L	0.78-1.79 µg/g Cr Premeno-luteal or ERT
Estrone	2.85	2.27-5.22 µg/g Cr Premeno-luteal or ERT
Estriol	0.83	0.78-1.98 µg/g Cr Premeno-luteal or ERT
E3/(E1+E2)	0.24 L	>0.3 (> median value)
2-OH Estradiol	0.21	0.17-0.70 µg/g Cr Premeno-luteal or ERT
2-OH Estrone	1.09	0.70-2.54 µg/g Cr Premeno-luteal or ERT
4-OH Estradiol	0.15	0.10-0.18 µg/g Cr Premeno-luteal or ERT
4-OH Estrone	0.47	0.17-0.47 µg/g Cr Premeno-luteal or ERT
16α-OH Estrone	0.31 L	0.35-1.07 µg/g Cr Premeno-luteal or ERT
2-OH (E1 + E2)/16-α-OH E1	4.19	1.29-5.49 Premeno-luteal or ERT
2-MeO Estradiol	0.06	0.03-0.08 µg/g Cr Premeno-luteal or ERT
2-MeO Estrone	0.51	0.26-0.68 µg/g Cr Premeno-luteal or ERT
2-MeO E1/2-OH E1	0.47 H	0.21-0.38 Premeno-luteal or ERT
4-MeO Estradiol	0.05 H	<0.04 µg/g Cr
4-MeO Estrone	0.12 H	<0.04 µg/g Cr
4-MeO E1/4-OH E1	0.26 H	0.05-0.13 Premeno-luteal or ERT
4-MeO E2/4-OH E2	0.33 H	0.10-0.29 Premeno-luteal or ERT
Bisphenol A	<dl L	1.5-4.5 µg/g Cr Postmenopausal

Hormone Insights Test (HIT)

Powered by the Advanced Urine Hormone Metabolites Test by ZRT

ZRT LABORATORY

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When to re-test

Re-testing is generally recommended at **3 – 6 months**

What if I don't see changes, or they get worse?

- See previous FIT test considerations
- Consider ACTUAL client compliance
- Consider where you are in your support protocol
- Consider increased stress and other lifestyle or health factors
- Consider running a stool / SIBO test
- Consider GP referral or involvement

KBMO DIAGNOSTICS

Sources from food

- Sulforaphane is a potent antioxidant compound found primarily in raw cruciferous vegetables, with broccoli sprouts being the most concentrated source (up to 50 times more than mature broccoli).
- Other top sources include broccoli, kale, Brussels sprouts, cabbage, cauliflower, and bok choy.
- It is activated when these veggies are chewed or chopped.
- Adding mustard seed powder to cooked broccoli or other cruciferous vegetables can increase sulforaphane bioavailability by over four times. Cooking destroys the enzyme myrosinase needed to activate sulforaphane; mustard provides a fresh source of this enzyme to create a potent, anti-cancer, and antioxidant effect.

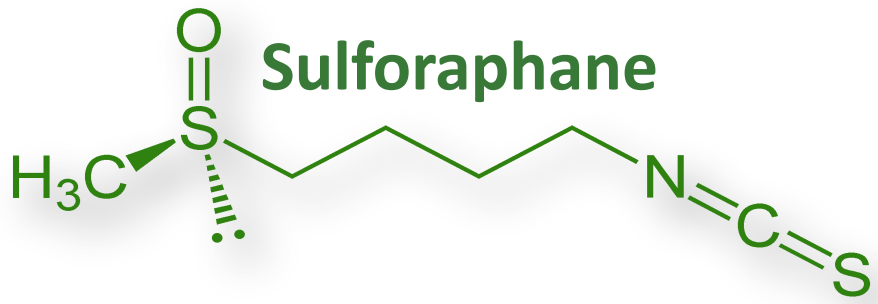
KBMO DIAGNOSTICS

Sulforaphane–yielding product

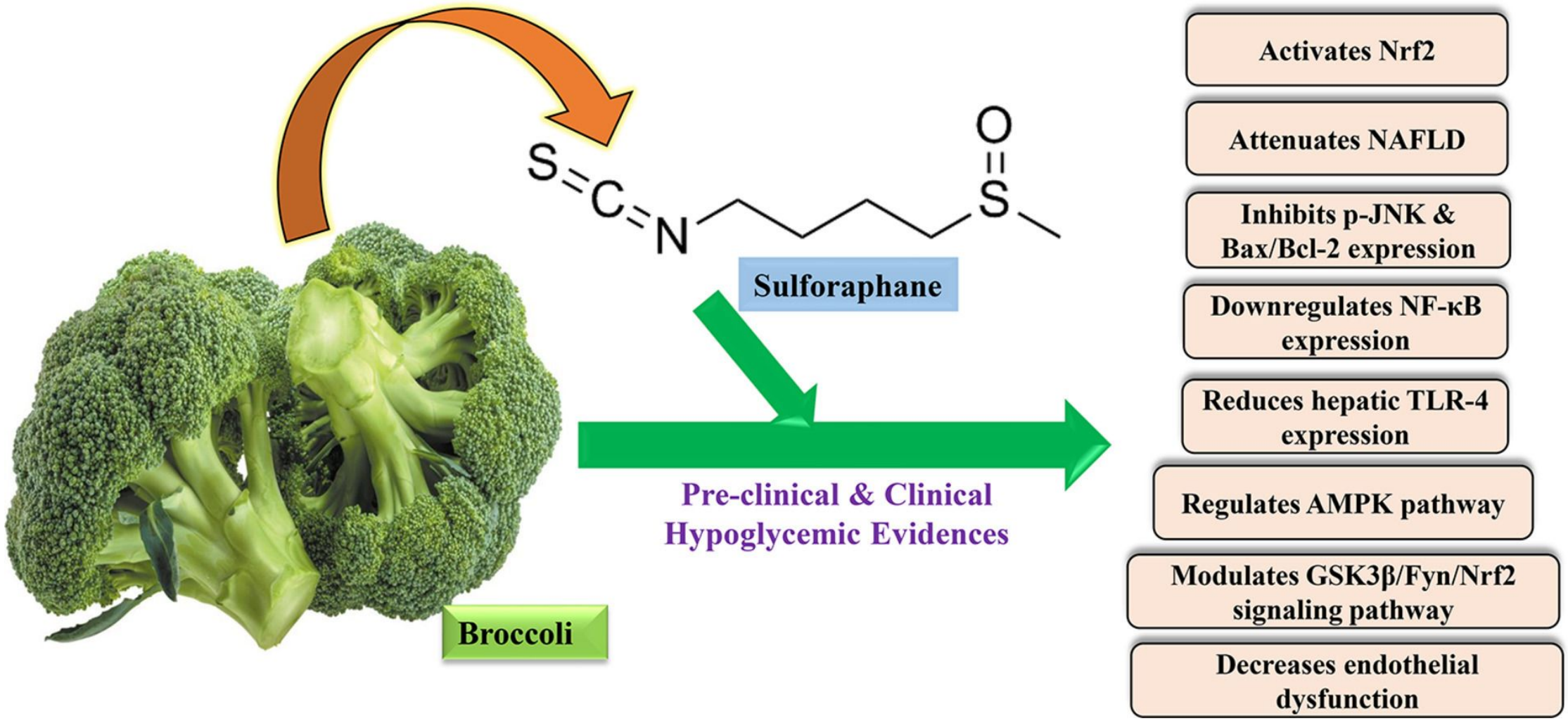
Supplement Facts

Serving Size: 1 Capsule
Servings Per Container: 60

	Amount Per Serving	%DV*
Selenium (as l-selenomethionine)	25 mcg	45%
Broccoli Sprout Powder (EnduraCell®)	700 mg	**
(Brassica oleracea var. italica)		



KBMO DIAGNOSTICS



https://www.sciencedirect.com/science/article/pii/S2667031323000271

KBMO DIAGNOSTICS

The gut is the foundation of systemic health

It influences immune regulation, detoxification, hormone balance, and brain function.

The KBMO Gut Barrier Panel can help you identify hidden dysfunction, including silent immune activation and can help you monitor whether Sulforaphane is helping your client

Detect early signs of chronic inflammation, IP or dysbiosis

Personalise support strategies, beyond symptom relief

Track real clinical outcomes through follow-up testing

KBMO DIAGNOSTICS

Take home

"Sulforaphane is a potent antioxidant and anti-inflammatory compound derived from cruciferous vegetables like broccoli sprouts. It activates the Nrf2 pathway, providing strong anti-cancer, detoxification, gut and neuroprotective benefits, while supporting heart health, reducing skin UV damage, and potentially aiding in managing autism symptoms and type 2 diabetes."

KBMO DIAGNOSTICS

Thank You

www.kenko-health.com for EU distribution of KBMO and NutriDyn

Kenko Health

KBMO DIAGNOSTICS

Thank You

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KBMO DIAGNOSTICS

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