

Casual Friday Series

# Winning the War on Pain

[BIOGENETIX.COM](http://BIOGENETIX.COM)



# Disclaimer

- *Information in this presentation is not intended to diagnose, treat, reverse, cure, or prevent any disease. While this presentation is based on medical literature, findings, and text, The following statements have not been evaluated by the FDA.*
- *The information provided in this presentation is for your consideration only as a practicing health care provider. Ultimately you are responsible for exercising professional judgment in the care of your own patients.*





(Lifestyle + Genetics) x Time = Chronic Health Condition

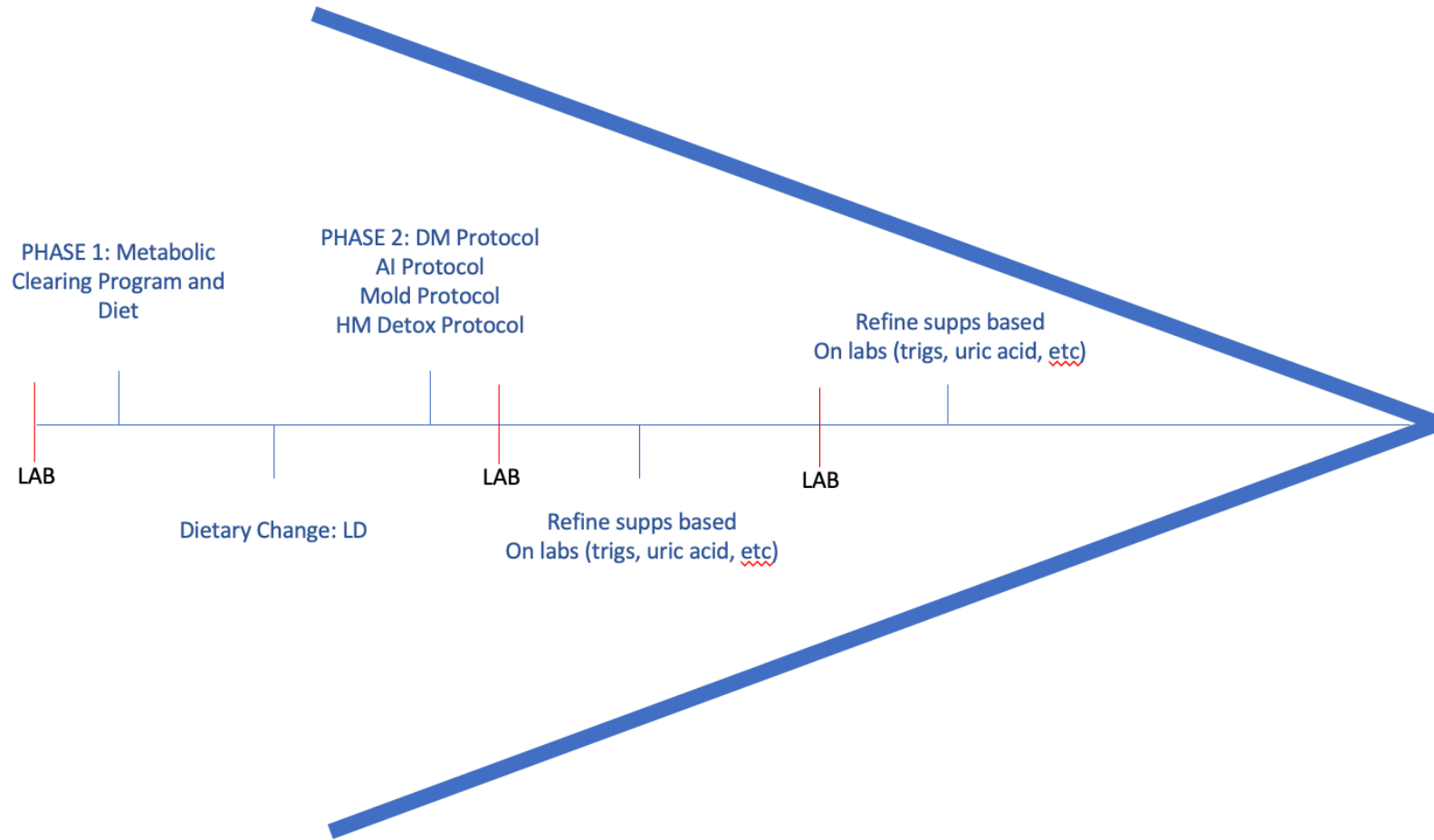




**(Lifestyle + Genetics) x Time = Chronic Health IMPROVEMENT**



# Supplement and Diet Protocols



Retest a lab at least every 60 days.

85% of patients will improve with basic structures and healthy eating.

% of problem analysis: this is what the cleanse is for.

General  Fine Tune

## PATTERNS

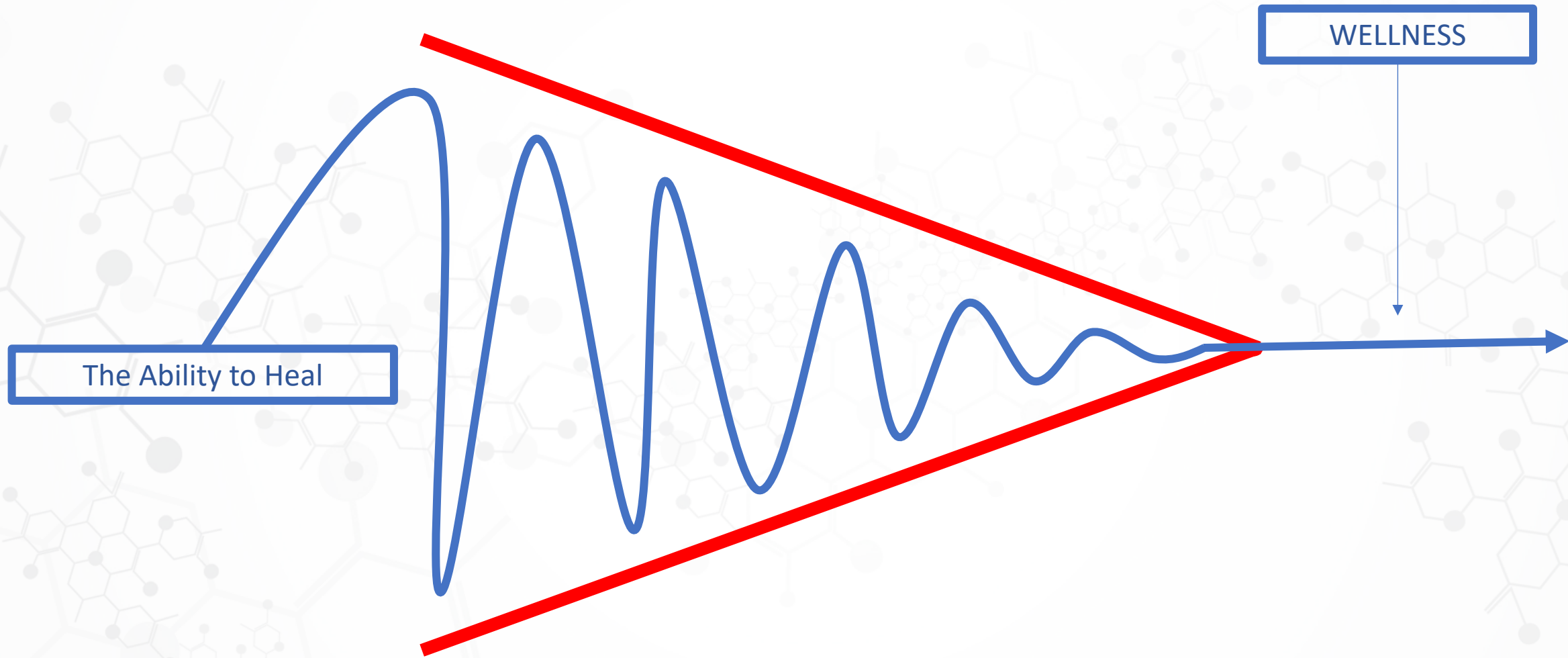
Anemias  
Blood Sugar Dysregulation  
Infections/Stressors  
Biotoxin  
Net Detoxification  
Thyroid Disorders  
Acid/Base  
Hormone Sequestering  
Genetic SNPs  
Inflammatory Regulation  
Auto Immune Responses  
Trophic Needs  
Sympathetic/Para  
Hormone Dysregulation  
Toxicity  
Organ Dysfunction

## PROTOCOL

Blood Sugar Dysregulation  
  
Net Detoxification  
  
Hormone Sequestering  
  
Inflammatory Regulation  
  
Trophic Needs  
Sympathetic/Para  
Hormone Dysregulation



# Building Protocols



The Ability to Heal

WELLNESS



## PATTERNS

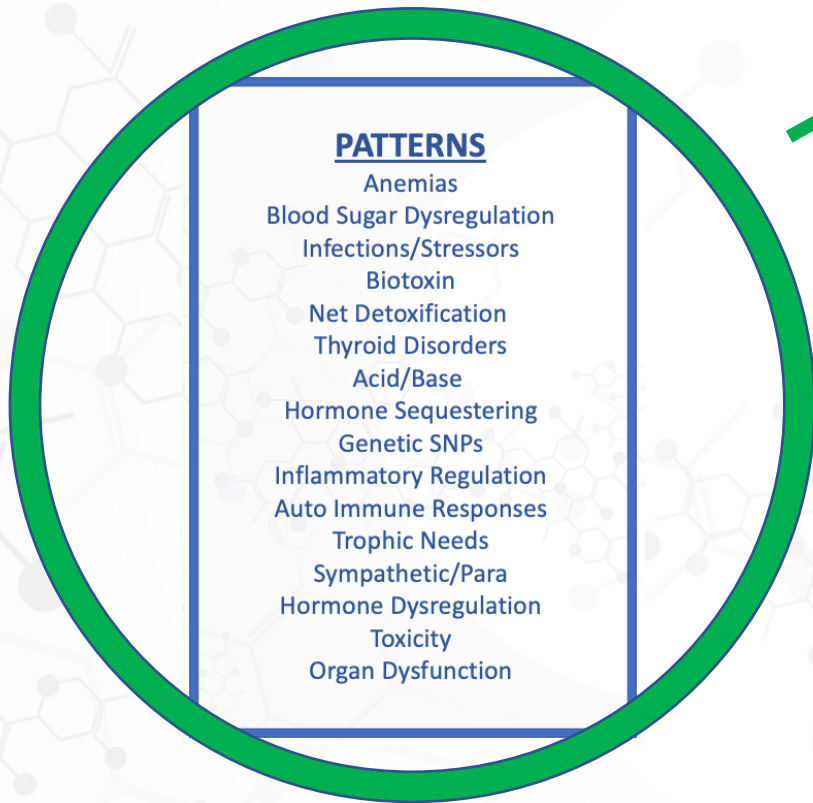
Anemias  
Blood Sugar Dysregulation  
Infections/Stressors  
Biotoxin  
Net Detoxification  
Thyroid Disorders  
Acid/Base  
Hormone Sequestering  
Genetic SNPs  
Inflammatory Regulation  
Auto Immune Responses  
Trophic Needs  
Sympathetic/Para  
Hormone Dysregulation  
Toxicity  
Organ Dysfunction

## PROTOCOL

Blood Sugar Dysregulation  
  
Net Detoxification  
  
Hormone Sequestering  
  
Inflammatory Regulation  
  
Trophic Needs  
Sympathetic/Para  
Hormone Dysregulation







## Zeb's Offer: Order 21-Day Metabolic Clearing Program

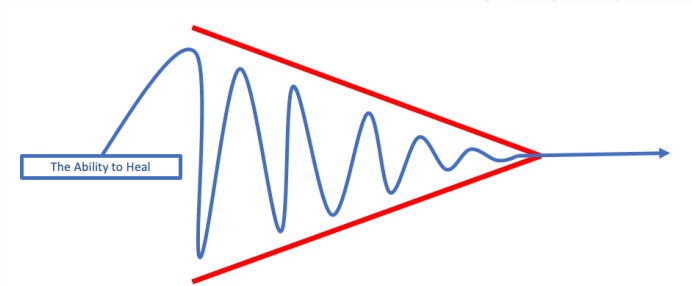


### Applied Blood Chemistry – **FREE**

- Through the end of October
- 12 Hour Course
- Learn to ID the patterns
- Get exposed to Functional Analysis
- MSRP \$799
- CE-not available in this format



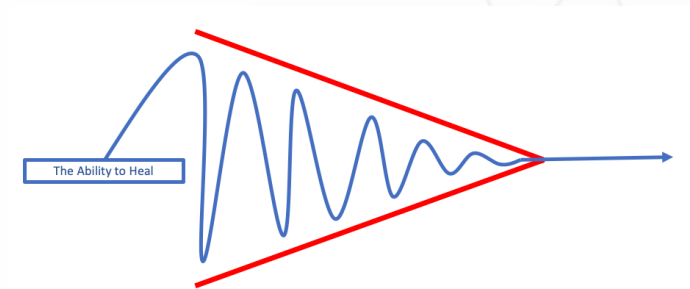
# Pain Classification: Acute or Chronic



## Regarding Classification...

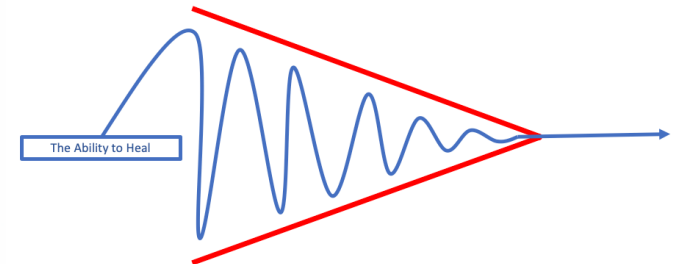
- Remember, FM practitioners don't chase names, diagnoses, or syndromes.
- We are detectives, detectives use descriptions.
- Descriptions yield Classification.
- Classification directs organization.
- Organization promotes repeatable results.

\*\*\* Repeatability is KEY. Predictability in the outcome.

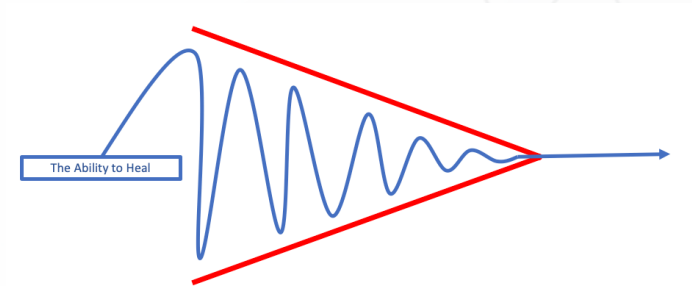


The main type of pain we'll talk about today, under the CHRONIC heading:

## Neuropathic Pain



**Neuropathic pain** is **pain** caused by damage or disease affecting the somatosensory nervous system. **Neuropathic pain** may be associated with abnormal sensations called dysesthesia or **pain** from normally non-**painful** stimuli (allodynia).

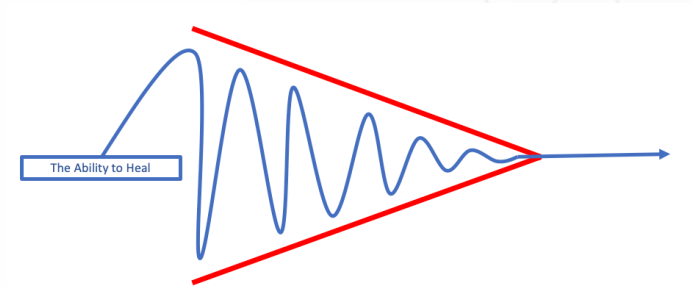


# Where Modern Medicine is Currently....

“The opioid epidemic could kill as many as 650,000 people in the next decade.”

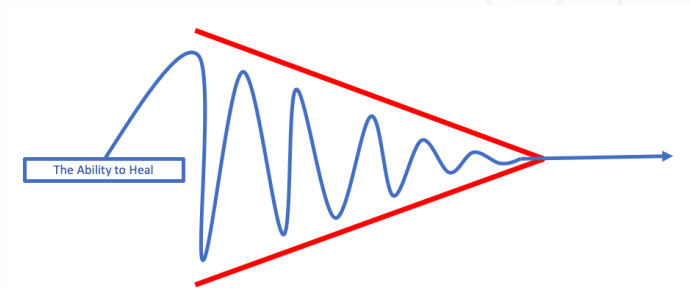
“Children of the opioid epidemic are flooding foster homes...America turns a blind eye.”

“OHIO: City morgue’s are full, thanks to the opioid crisis.”



- Come for the pain relief but stay for the pleasure.
- What we are talking about today is for those that have YET to be placed on the medical-heroin bandwagon (and those that want off!)

**“1/12 doctors has received money from drug companies marketing prescription opioid medications” - American Journal of Public Health**

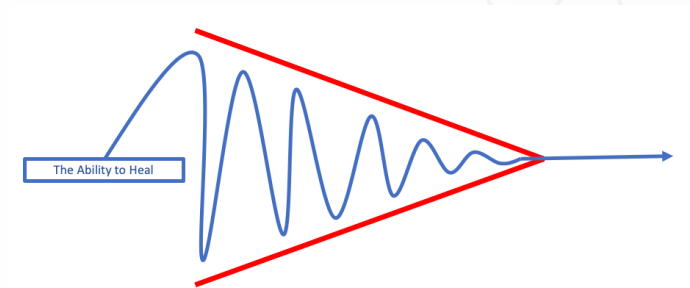


# Neuropathic Pain “Switch” Identified

**Endogenous adenosine A3 receptor activation selectively alleviates persistent pain states**

Joshua W. Little Amanda Ford Ashley M. Symons-Liguori Zhoumou Chen Kali Janes  
Timothy Doyle Jennifer Xie Livio Luongo Dillip K. Tosh Sabatino Maione Kirsty Bannister  
Anthony H. Dickenson Todd W. Vanderah Frank Porreca Kenneth A. Jacobson Daniela  
Salvemini

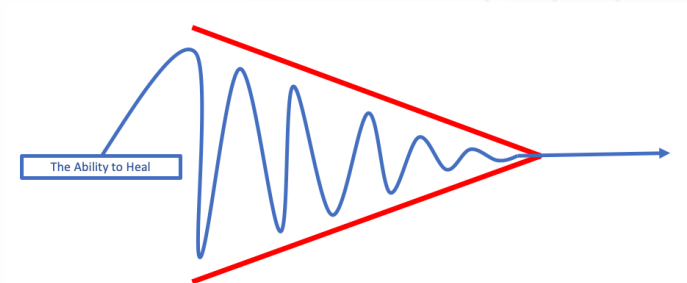
Further examination revealed that A3AR activation reduced spinal cord pain processing by decreasing the excitability of spinal wide dynamic range neurons and producing supraspinal inhibition of spinal nociception through activation of serotonergic and noradrenergic bulbospinal circuits.



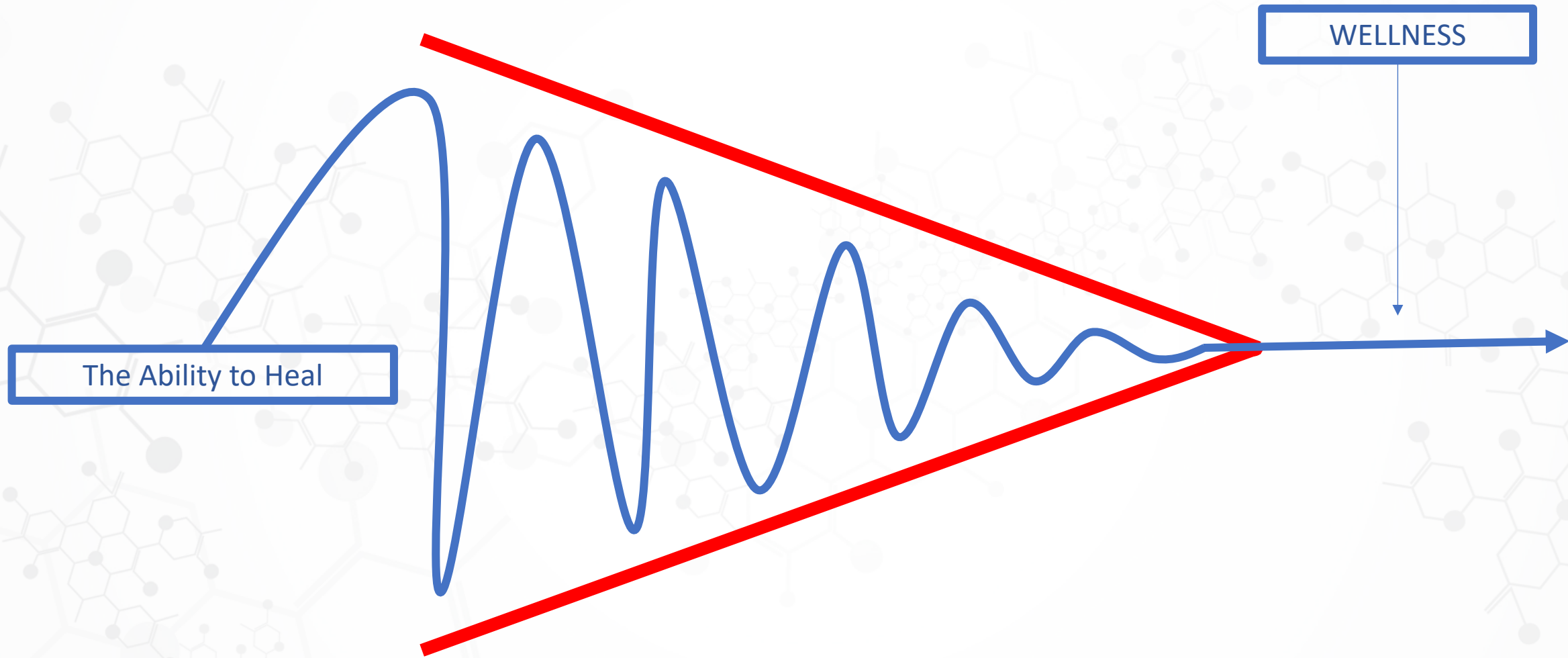


What activates the A3 Receptor?

**ADENOSINE**



# Building Protocols



The Ability to Heal

WELLNESS

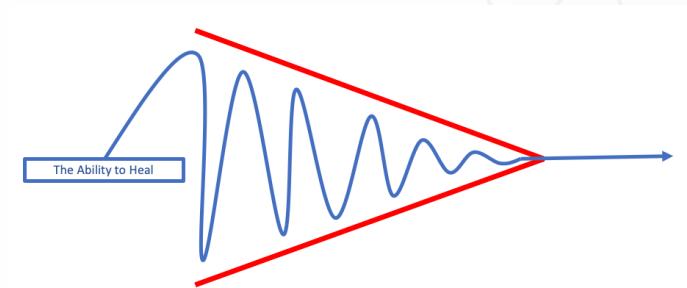


# Modern Medicine...

- Methotrexate is an A3Ar agonist drug.

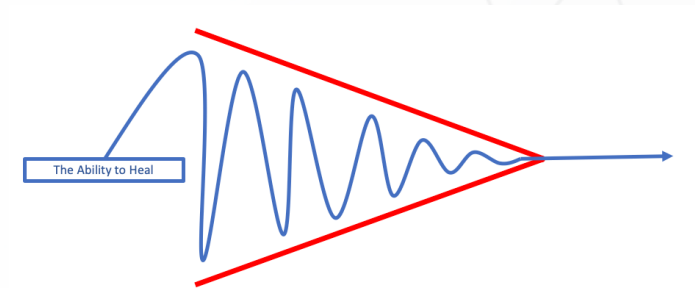
**Methotrexate (MTX)**, formerly known as **amethopterin**, is a chemotherapy agent and immune system suppressant.<sup>[1]</sup> It is used to treat cancer, autoimmune diseases, ectopic pregnancy, and for medical abortions.

Common side effects include nausea, feeling tired, fever, increased risk of infection... low white blood cell counts, and breakdown of the skin inside the mouth. Other side effects may include liver disease, lung disease, lymphoma, and severe skin rashes.



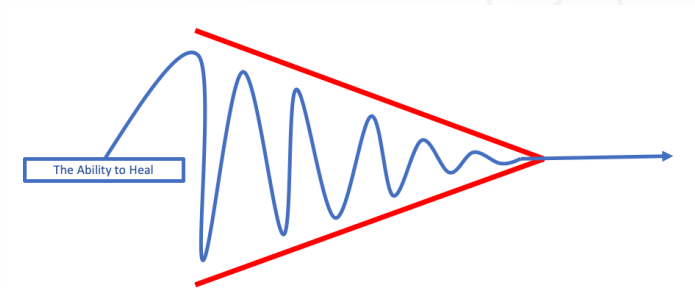
# Why is A3 agonist action loaded with side effects?

- Agonistic action means that you're spending Adenosine at a faster rate, but the overall adenosine levels don't change...
  - nausea, tired, fever, risk of infection, liver disease, lymphoma, etc.
- COULD IT BE THAT ADENOSINE IS ***THAT*** IMPORTANT?



# Adenosine?

- Adenosine is made up of adenine attached to a ribose sugar molecule (ribofuranose) moiety.
- Used in energy metabolism (ATP), yes, BUT it's the use in Signal TRANSDUCTION from cell to cell as cAMP that should excite us. This is a **key** in modulating pain stimuli for your patient base.

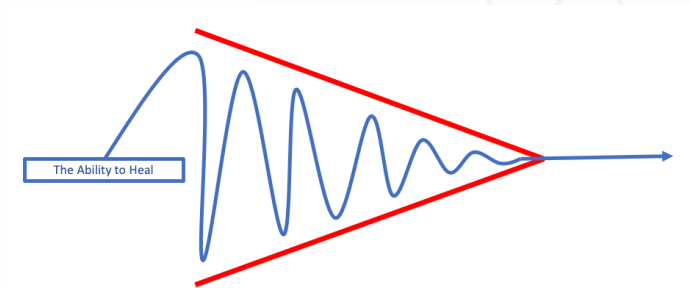


# Can we measure Adenosine?

Efficiently?

**Adenosine deaminase** (also known as **adenosine** aminohydrolase, or **ADA**) is an enzyme (EC 3.5.4.4) involved in purine metabolism. It is needed for the breakdown of **adenosine** from food and for the turnover of nucleic acids in tissues. Its primary function in humans is the development and maintenance of the immune system.

Unfortunately, this is most often measured in pleural fluid or pericardial fluid. I dare you to send your patient to the lab to draw that one!

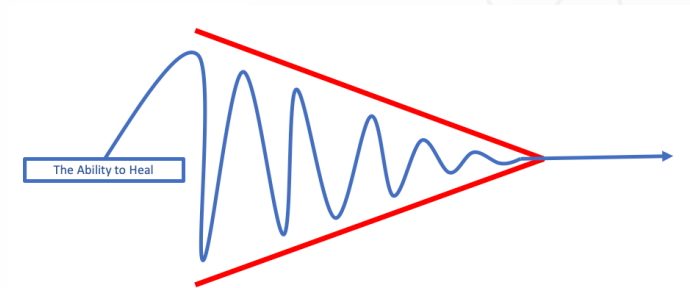


# Identify the reflection...

**A(1) and A(3) adenosine receptors alter glutathione status in an organ-specific manner and influence the changes after inhibition of gamma-glutamylcysteine ligase.**

Conte C1, Grottelli S, Prudenzi E, Bellezza I, Fredholm BB, Minelli A.

This study determined organ glutathione levels and expression of two sub-units of gamma-glutamylcysteine ligase and the cationic x(c)-transporter and found that deletion of one or both adenosine receptors influenced the responses in an organ-specific manner. **The lack of A(1) and A(3) adenosine receptors is related to decreased basal glutathione content** and down-regulation of gamma-glutamylcysteine ligase sub-units in several organs.



## PATTERNS

Anemias  
Blood Sugar Dysregulation  
Infections/Stressors  
Biotoxin  
Net Detoxification  
Thyroid Disorders  
Acid/Base  
Hormone Sequestering  
Genetic SNPs  
Inflammatory Regulation  
Auto Immune Responses  
Trophic Needs  
Sympathetic/Para  
Hormone Dysregulation  
Toxicity  
Organic Acid Shifts

## PROTOCOL





# Identify the reflection...

## Indicators of Detoxification

### Glutathione

58 Pyroglutamic \* 10 - 33 H 48

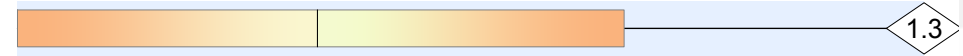
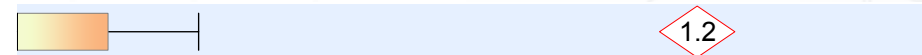
59 2-Hydroxybutyric \* 0.03 - 1.8 H 3.2

### Ammonia Excess

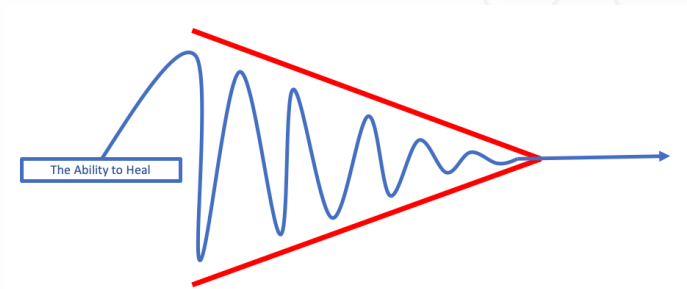
60 Orotic 0.06 - 0.54 H 1.2

### Aspartame, salicylates, or GI bacteria

61 2-Hydroxyhippuric  $\leq 1.3$  1.3



\* A high value for this marker may indicate a Glutathione deficiency.



### Glycolytic Cycle Metabolites

22	Lactic	≤ 48		35	
23	Pyruvic	≤ 9.1		8.1	

### Mitochondrial Markers - Krebs Cycle Metabolites

24	Succinic	≤ 9.3		7.2	
25	Fumaric	≤ 0.94	H	1.7	
26	Malic	0.06 - 1.8	H	3.2	
27	2-Oxoglutaric	≤ 35	H	49	
28	Aconitic	6.8 - 28		19	
29	Citric	≤ 507	H	1 653	

### Mitochondrial Markers - Amino Acid Metabolites

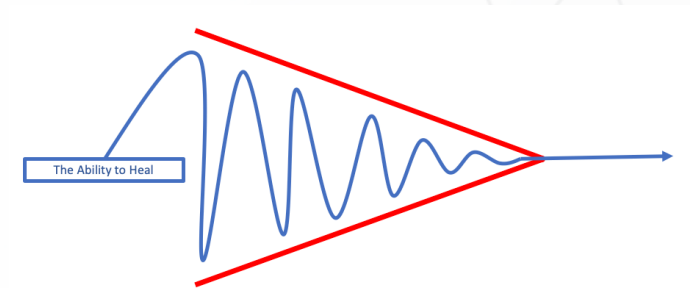
30	3-Methylglutaric	≤ 0.76		0.49	
31	3-Hydroxyglutaric	≤ 6.2	H	8.7	
32	3-Methylglutaconic	≤ 4.5		2.1	



# FM - type Pain Syndromes

Oxidative stress, mitochondrial dysfunction and, inflammation common events in skin of patients with Fibromyalgia. Sánchez-Domínguez B, Bullón P et al. Mitochondrion. 2015 Mar;21:69-75.

Recent studies have shown some evidence demonstrating that oxidative stress, mitochondrial dysfunction and inflammation may have a role in the pathophysiology of fibromyalgia.



## Neurotransmitter Metabolites

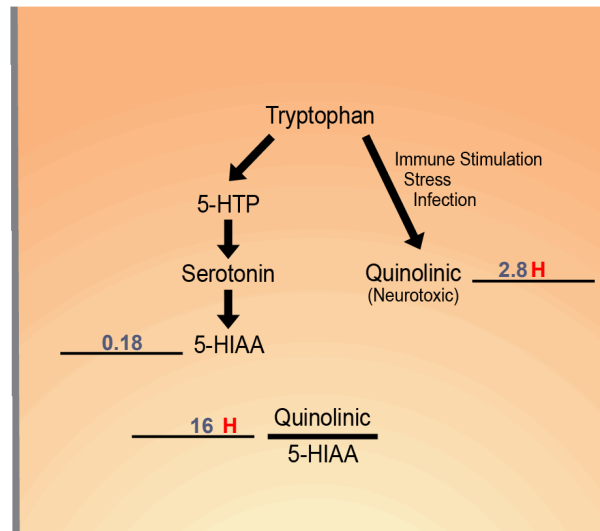
### Phenylalanine and Tyrosine Metabolites

33	Homovanillic (HVA) <i>(dopamine)</i>	0.39 - 2.2		2.2	
34	Vanillylmandelic (VMA) <i>(norepinephrine, epinephrine)</i>	0.53 - 2.2		1.6	
35	HVA / VMA Ratio	0.32 - 1.4		1.4	

### Tryptophan Metabolites

36	5-Hydroxyindoleacetic (5-HIAA) <i>(serotonin)</i>	≤ 2.9		0.18	
37	Quinolinic	0.52 - 2.4	<b>H</b>	2.8	
38	Kynurenic	0.12 - 1.8		1.1	
39	Quinolinic / 5-HIAA Ratio	≤ 2.5	<b>H</b>	16	

## Neurotransmitter Metabolism Markers



## PATTERNS

Anemias  
Blood Sugar Dysregulation  
Infections/Dysbiosis  
Biotoxin  
Net Detoxification  
Thyroid Disorders  
Acid/Base  
Hormone Sequestering  
Genetic SNPs  
Inflammatory Regulation  
Auto Immune Responses  
Trophic Needs  
Sympathetic/Para  
Hormone Dysregulation  
Toxicity  
Organic Acid Shifts

## PROTOCOL

Infections/Dysbiosis  
Net Detoxification

Inflammatory Regulation

Organic Acid Shifts



# Destroying Pain *Without* Addiction



# The Future of Medicine: Glutathione and PC?

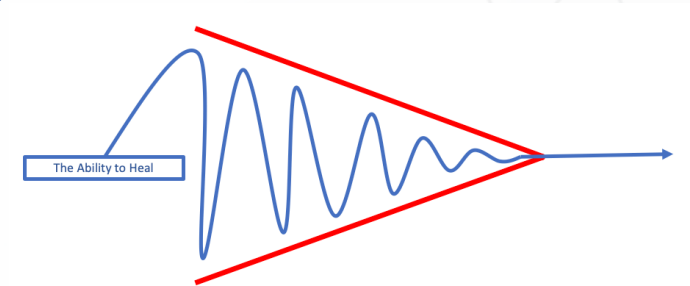
Biochem Pharmacol. 2015 Sep 15;97(2):215-23. doi: 10.1016/j.bcp.2015.07.007. Epub 2015 Jul 23.

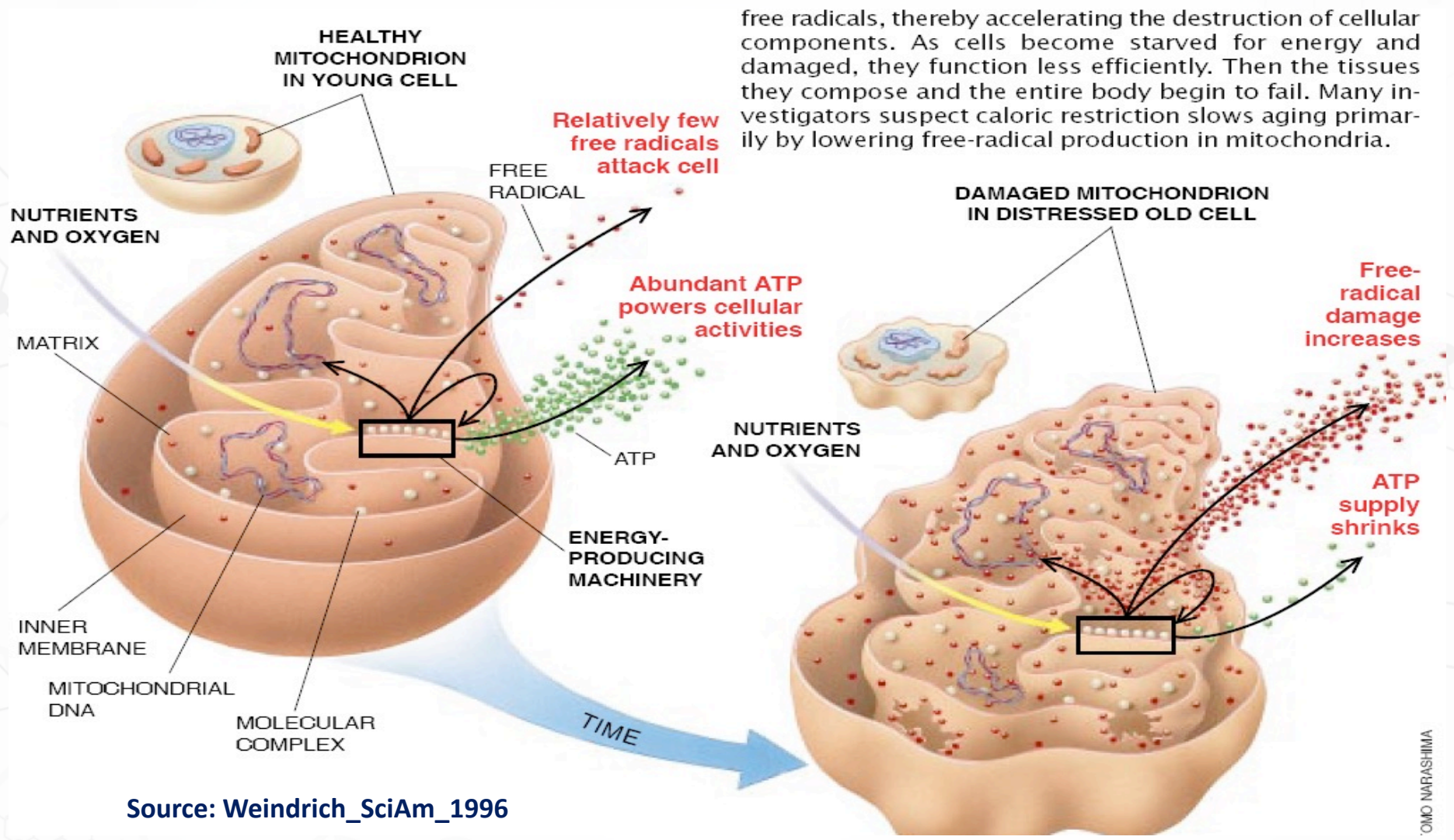
**Metabolic mapping of A3 adenosine receptor agonist MRS5980.**

Fang ZZ1, Tosh DK2, Tanaka N3, Wang H3, Krausz KW3, O'Connor R2, Jacobson KA4, Gonzalez FJ5.

Glutathione and PC inhibit utilization of the newest drug class that acts as an agonist to the A3 adenosine receptor.

Hilarious!





free radicals, thereby accelerating the destruction of cellular components. As cells become starved for energy and damaged, they function less efficiently. Then the tissues they compose and the entire body begin to fail. Many investigators suspect caloric restriction slows aging primarily by lowering free-radical production in mitochondria.

Source: Weindrich\_SciAm\_1996

©OMO NAPASHIMA





# GABA and Pain Transmission

One of the few cortical areas consistently activated by painful stimuli is the rostral agranular insular cortex (RAIC) where, as in other parts of the cortex, the neurotransmitter  $\gamma$ -aminobutyric acid (GABA) robustly inhibits neuronal activity.

Analgesia and hyperalgesia from GABA-mediated modulation of the cerebral cortex. Luc Jasmin, Samuel D. Rabkin, Alberto Granato, Abdennacer Boudah, Peter T. Ohara. *Nature* **424**, 316–320 (2003)



# GABA and Pain Transmission

we show that changes in GABA neurotransmission in the RAIC can raise or lower the pain threshold—producing analgesia or hyperalgesia, respectively

Locally increasing GABA...produces lasting analgesia by enhancing the descending inhibition of spinal nociceptive neurons.

Analgesia and hyperalgesia from GABA-mediated modulation of the cerebral cortex. Luc Jasmin, Samuel D. Rabkin, Alberto Granato, Abdennacer Boudah, Peter T. Ohara. *Nature* **424**, 316–320 (2003)



# Moral of the story...

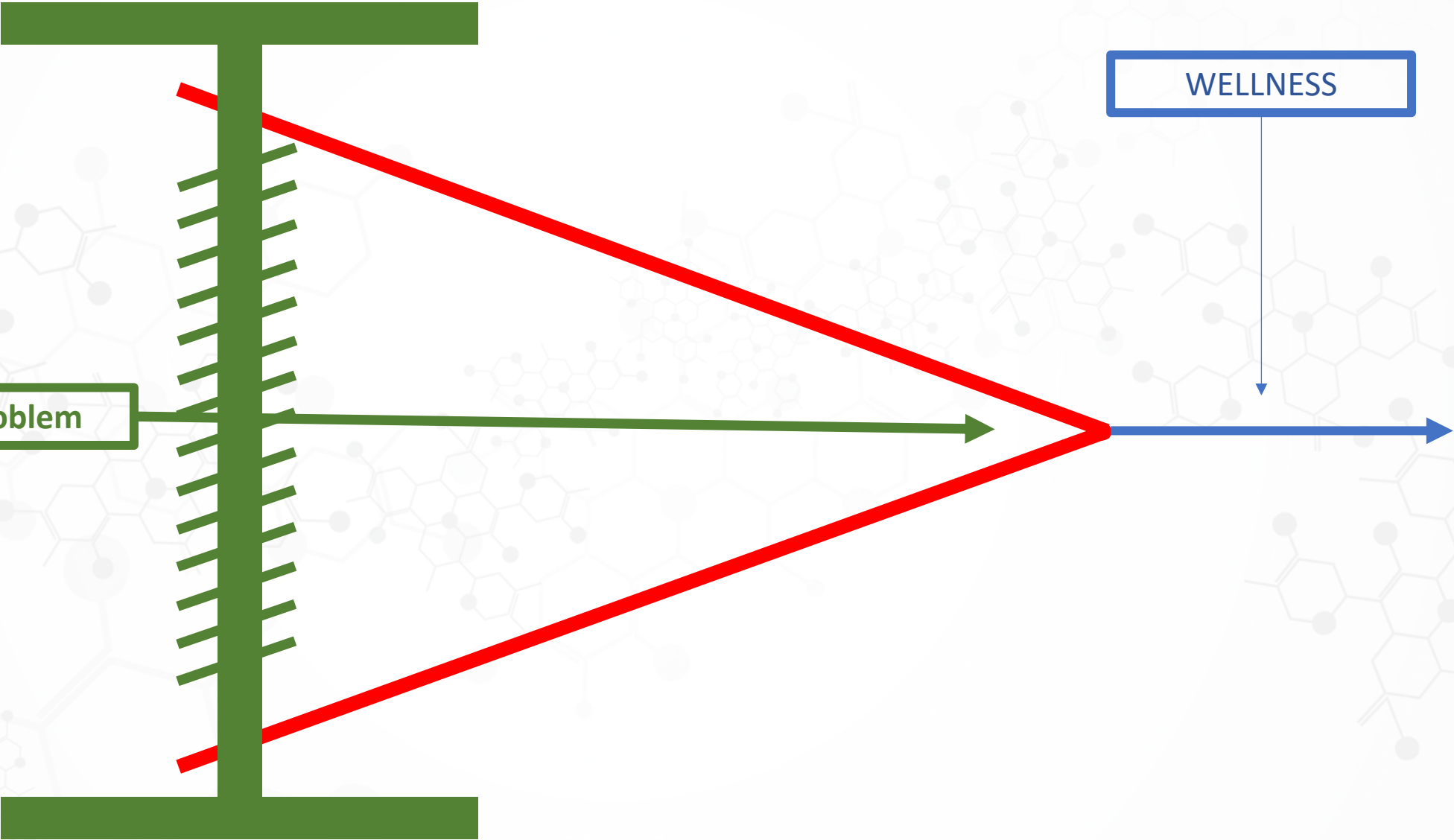
- GABA dampening of cortical pain transmission is a must!
- Any cell with a clearly delineated nucleus is going to have mitochondria.
- Mitochondria are the life centers of our physical body.
- ATP, the product of mitochondria, is the missing key in the realm of medical management of pain today.

Is there a protective mechanism at play?



Bookend the Problem

WELLNESS



# Destroying Pain *Without* Addiction



# Biogenetix: 833-525-0001



[zeb@biogenetix.com](mailto:zeb@biogenetix.com)



[kim@biogenetix.com](mailto:kim@biogenetix.com)

