"Nothing in this world can take the place of **persistence.**

Talent will not; nothing is more common than unsuccessful people with **talent.**

Genius will not; unrewarded genius is almost a **proverb.**

Education will not; the world is full of educated derelicts.

Persistence and **Determination** alone are **omnipotent.**

The slogan *"Press on"* has solved and always will solve the problems of the human race."

- Calvin Coolidge
American 30th President of the United States, 1872-1933

NEVER
NEVER
NEVER
GIVE UP

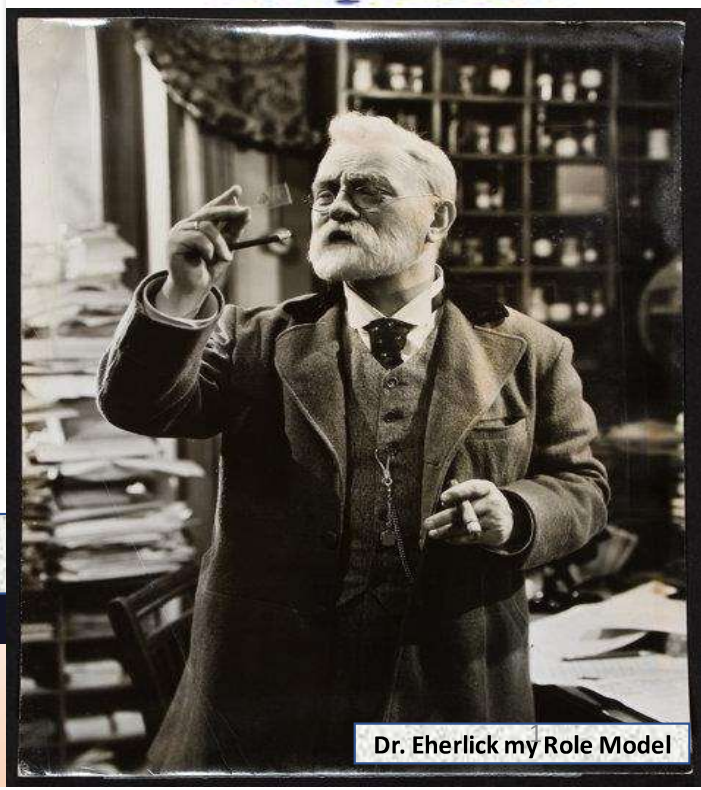
Winston Churchill

Patrick: The walking/talking lab rat

Disclosure:

Principle at K-Vitamins.com

"Everything should be made as simple as possible, but not simpler."



Dr. Eherlick my Role Model

Patient Zero (PT)

An N of 1

From Mid-November 2002 to date

The stopping and reversal of heart disease
by
10.2% in Score and Volume since 2012
As
Measured by Computed Tomography (CT)

A Precise, Concise, & Condensed

Controls Engineer's 50,000' view (it's all about connecting the dots)

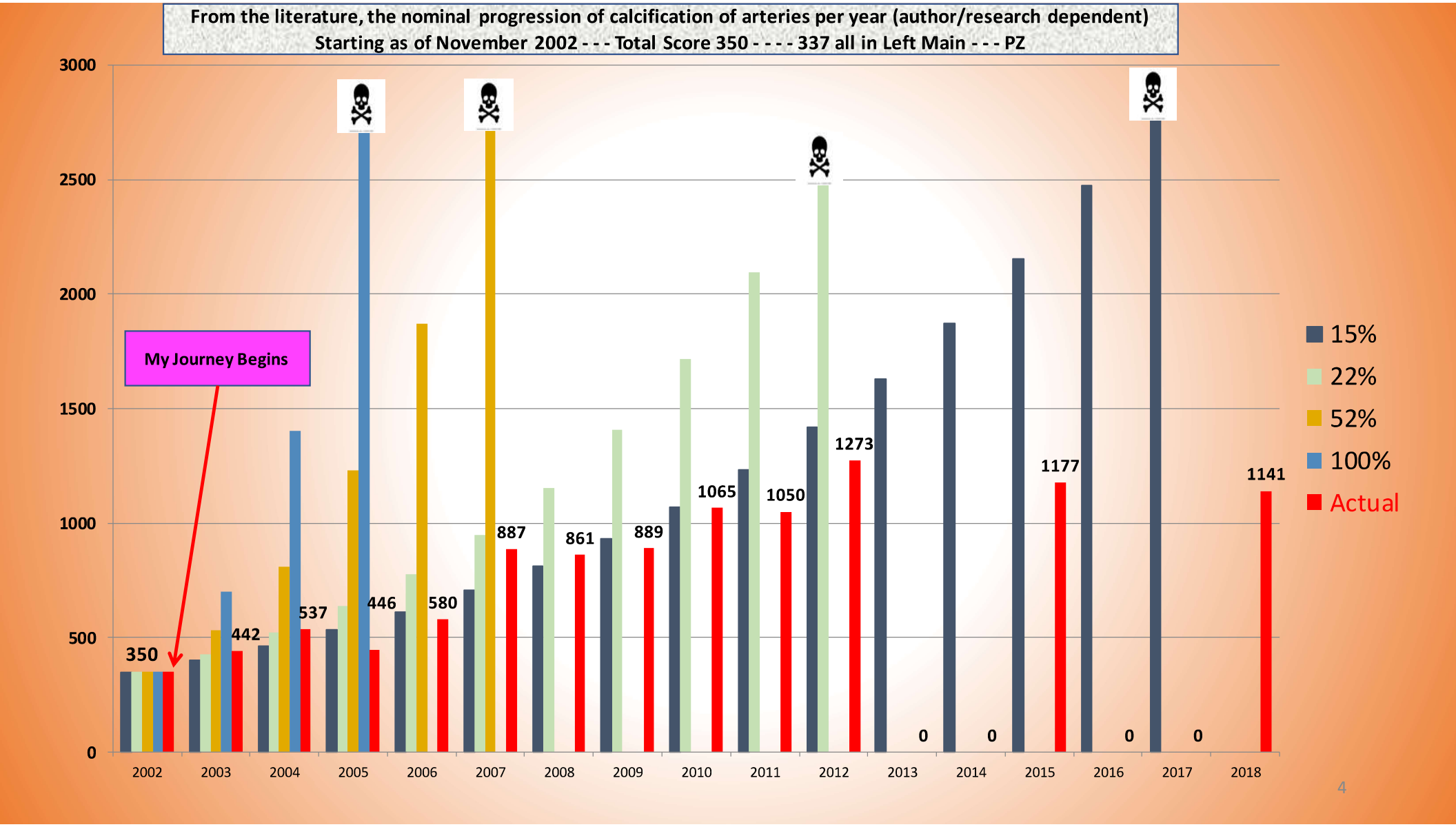
of

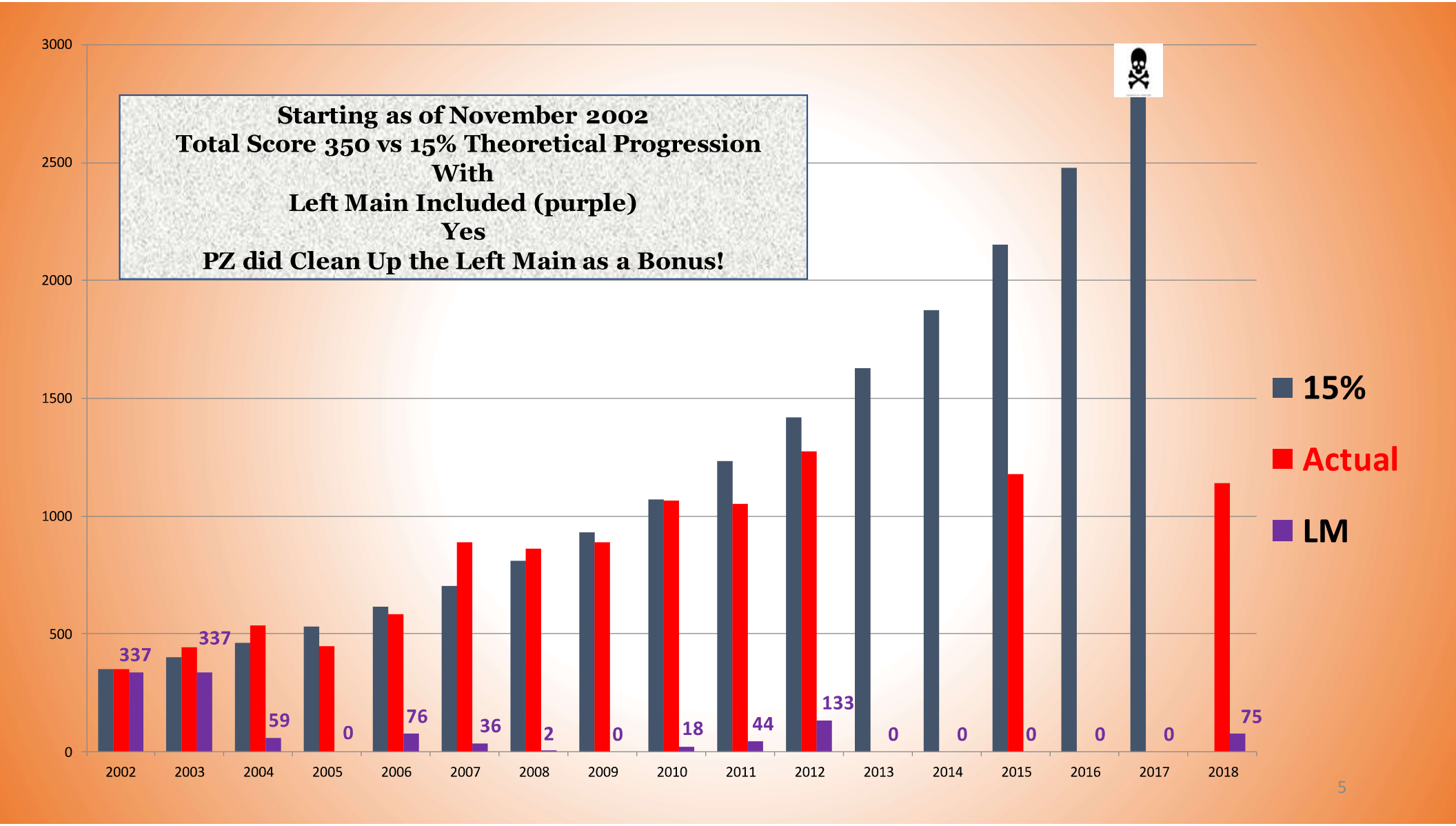
The Key Roles of

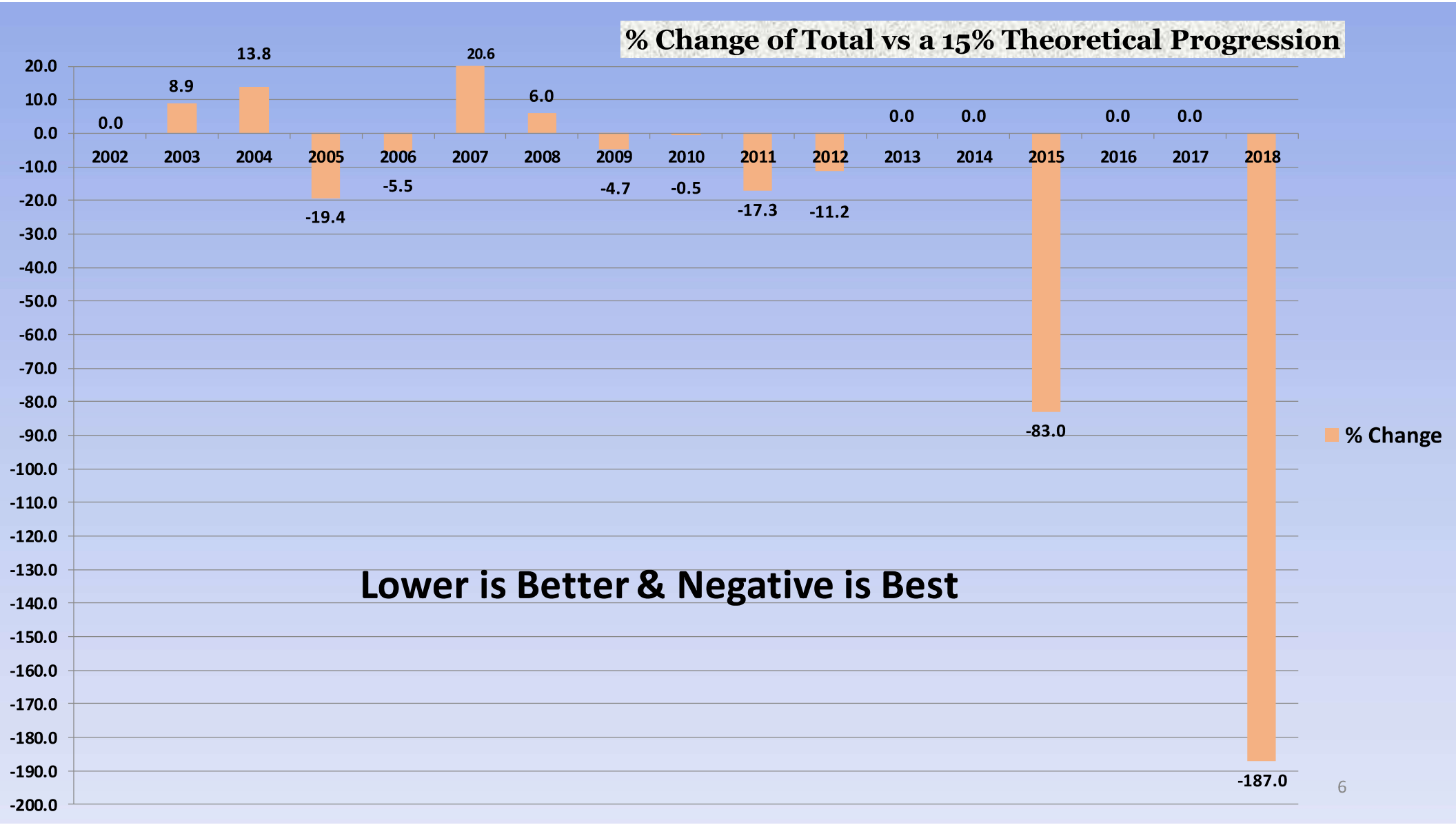
Vitamin K-1 and MK-7 and associated parallel Bio-Chemistry

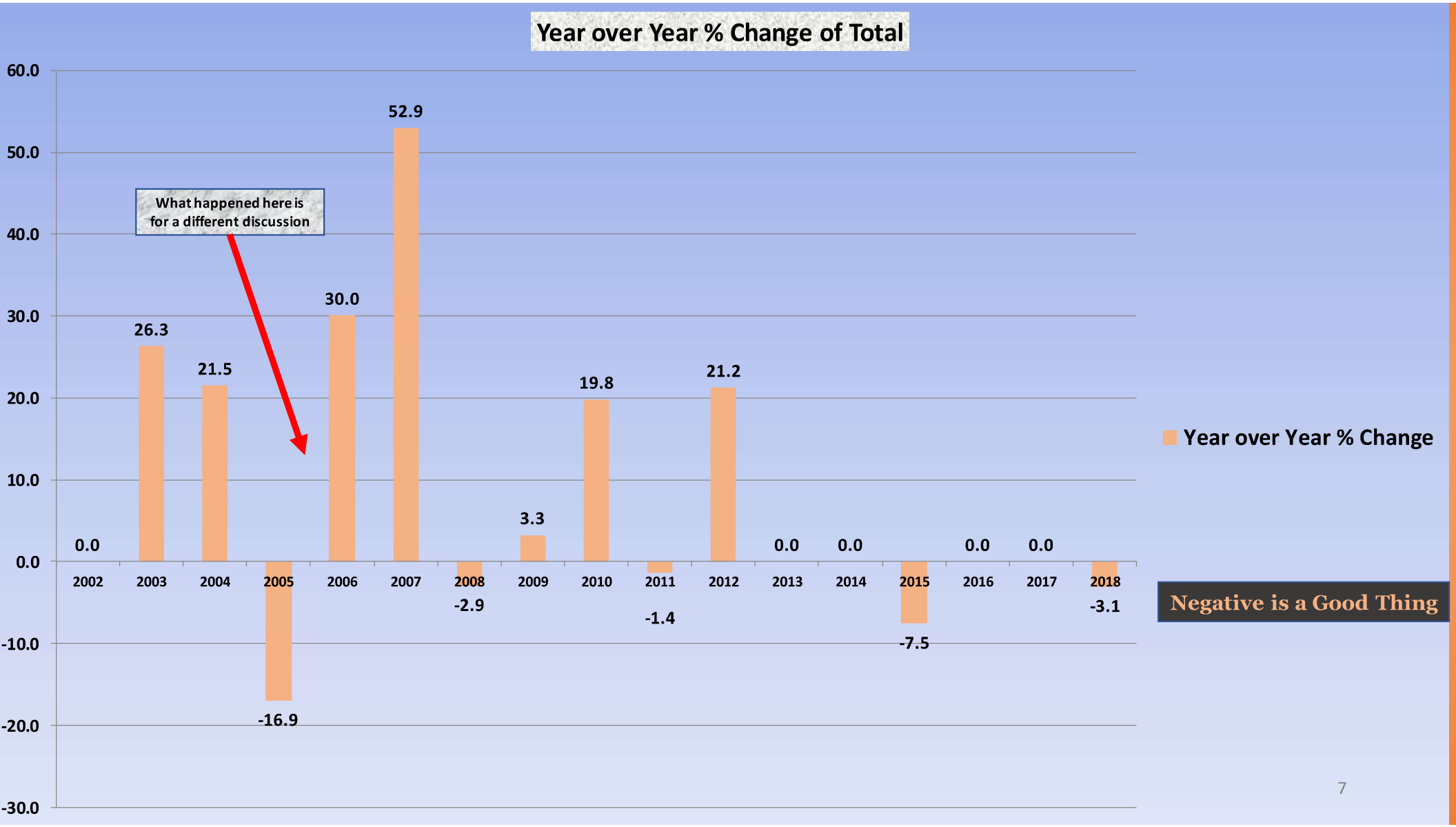
This 30 minute presentation represents the body of work to date of:

- **16,000 + hours of peer reviewed literature analysis by PT**
- **Exhaustive blood analysis during this same period of PT**
- **20+ CT scans of PT's heart**
  (neutral third party analysis of the scans during this same period)


From the literature, the nominal progression of calcification of arteries per year (author/research dependent)
Starting as of November 2002 - - - Total Score 350 - - - - 337 all in Left Main - - - PZ
3000
2500
2000
1500
1000
500
0
My Journey Begins
350
442
537
446
580
887
861
889
1065
1050
1273
0
0
1177
0
0
1141
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
15%
22%
52%
100%
Actual

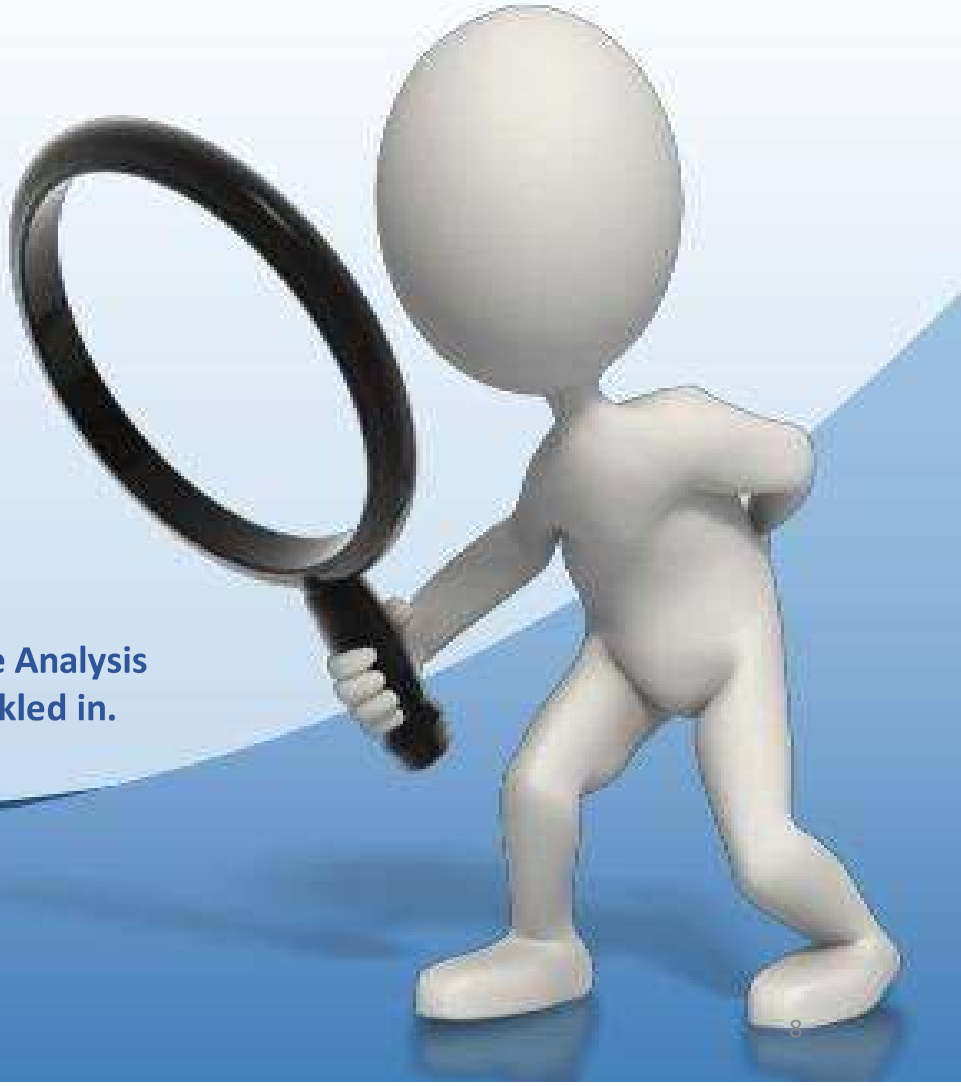

Starting as of November 2002
Total Score 350 vs 15% Theoretical Progression
With
Left Main Included (purple)
Yes
PZ did Clean Up the Left Main as a Bonus!
3000
2500
2000
1500
1000
500
0
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
337
337
59
0
76
36
2
0
18
44
133
0
0
0
0
0
75
15%
Actual
LM


% Change of Total vs a 15% Theoretical Progression
20.0
10.0
0.0
-10.0
-20.0
-30.0
-40.0
-50.0
-60.0
-70.0
-80.0
-90.0
-100.0
-110.0
-120.0
-130.0
-140.0
-150.0
-160.0
-170.0
-180.0
-190.0
-200.0
0.0
8.9
13.8
-19.4
-5.5
20.6
6.0
-4.7
-0.5
-17.3
-11.2
0.0
0.0
-83.0
0.0
0.0
-187.0
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
% Change
Lower is Better & Negative is Best


Year over Year % Change of Total
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
-20.0
-30.0
What happened here is for a different discussion
0.0
26.3
21.5
-16.9
30.0
52.9
-2.9
3.3
19.8
-1.4
21.2
0.0
0.0
-7.5
0.0
0.0
-3.1
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
Year over Year % Change
Negative is a Good Thing

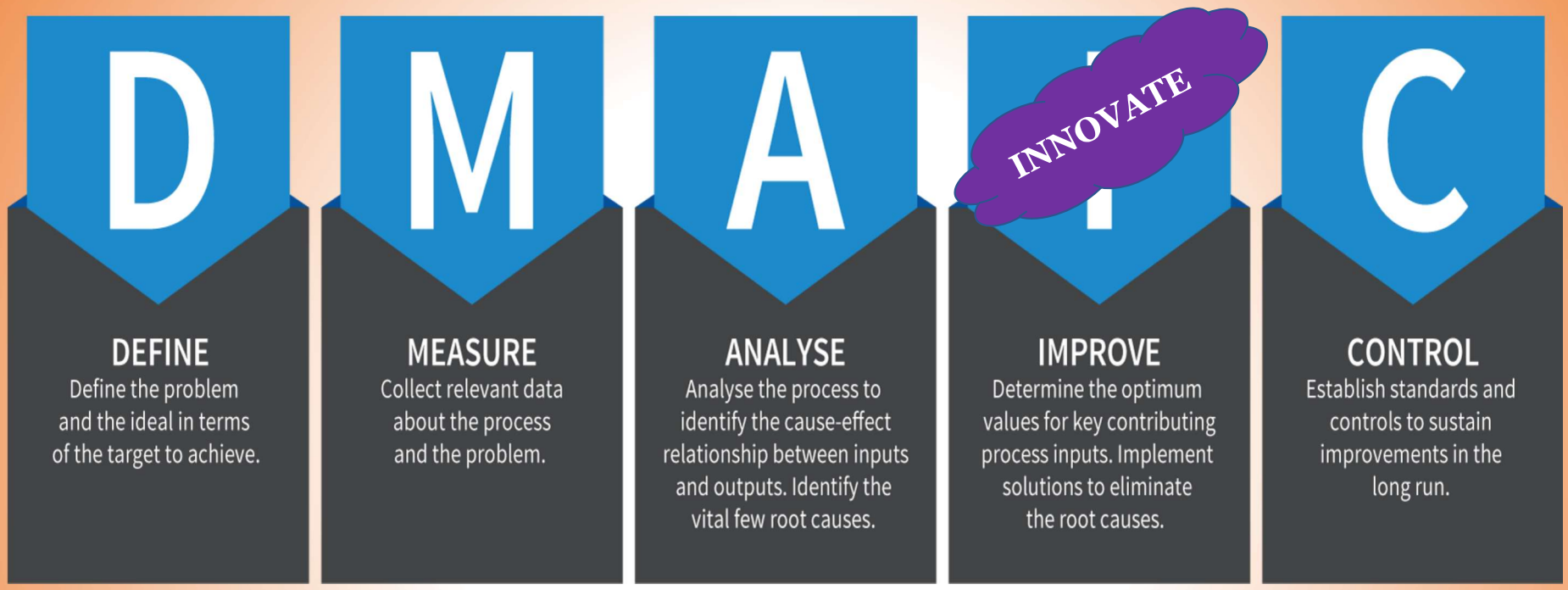
With the first question asked in November of 2002 being:

What Changed?



Followed by:
Who, When, Where, Why, & How
All based on Objective Evidence and Objective Analysis of the Data with some inferential logic sprinkled in.


A ROOT CAUSE YOU MUST FIND
IF A PROBLEM YOU WANT TO FIX...
memegenerator.net



Time, Temp, pH, Flow, Pressure, Chemical Consistency, Rheology

80/20 rule: 20, 4, 1.8, 0.36, 0.07

Cannot hit a target you cannot see and you cannot hit a target you do not have

Which Resulted in the Following Discoveries

DMAIC SIGNIFICANT DISCOVERIES BY APRIL 1 2003:

VITAMIN D
MAGNESIUM
SELENIUM
THYROID
GUT BACTERIA
CARBS
BAD FATS
SURFACE CHEMISTRY/SURFACE GEOMETRY
VITAMIN C
APOE
INFECTIONS (example: gum disease)
CoQ-10

SIGNIFICANT DMAIC DISCOVERIES IN JULY 2010:

VITAMIN K – ALL FORMS

Fetuin-A

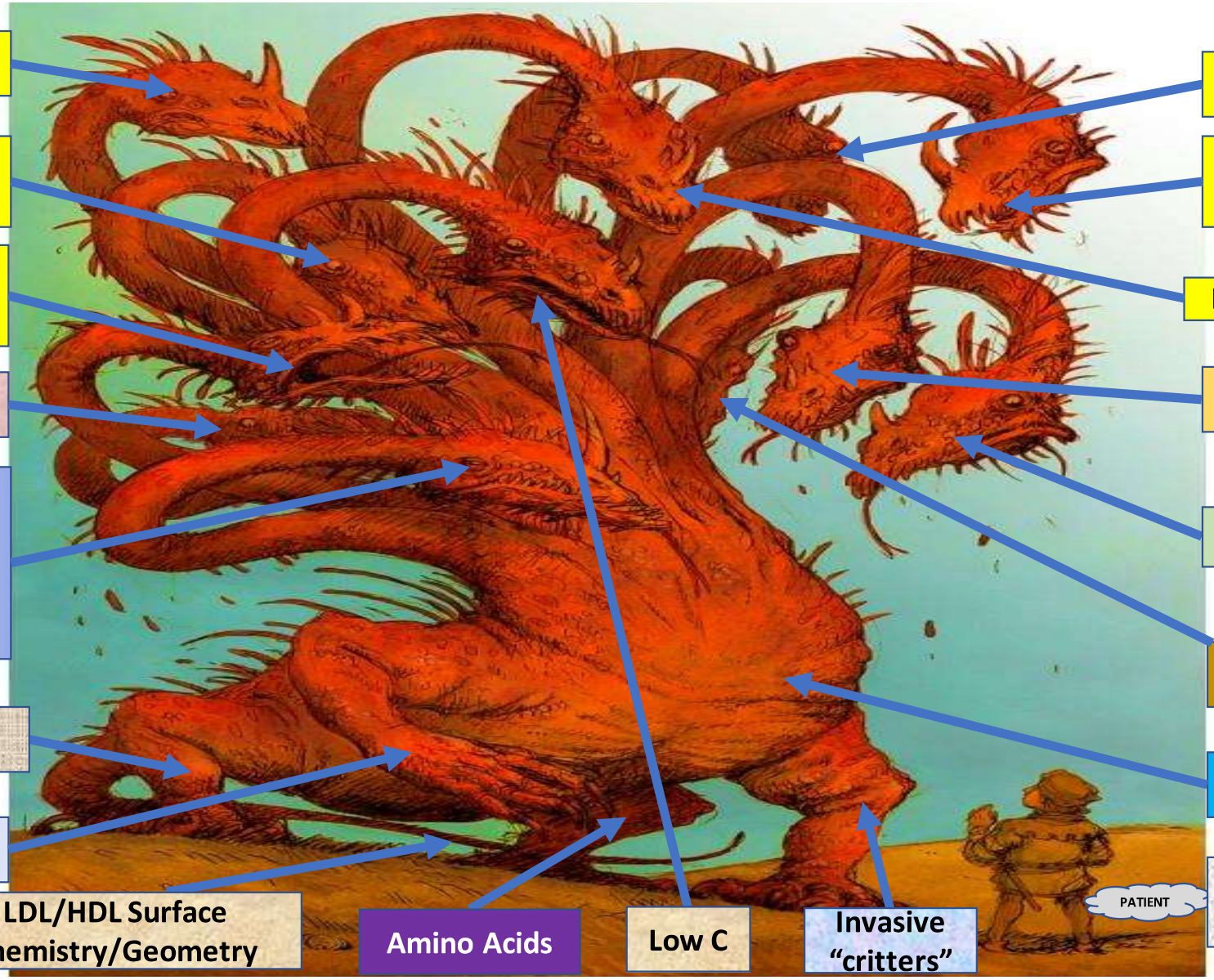
Which Resulted in the New Heart Disease Definition

2010 New Definition of the Problem:

Heart Disease Appears to Be:
Insufficient Carboxylation of Matrix Gla Proteins
resident on
Macrophages, Foam Cells, & VSMCs
Caused by
Insufficient MK-7 et.al.
Resident on or in
LDL, HDL, and VLDL

Impacted & Influenced by
Free T3 - - - Vitamin D - - - - Magnesium - - - - CoQ-10 - - - - Fetuin-A - - - - miRNA

Which Resulted in the New Pictorial Model


Low K
Fetuin-A Out of Range
APOE Status/miRNA
Insulin/Glucose
Exogenous Chemistry : Smoking/Statins/ Warfarin/Calcium/ Phosphorus
Autoimmune Issues
Hormones
LDL/HDL Surface Chemistry/Geometry
Amino Acids
Low C
Invasive "critters"
Low D/CoQ10
Free T3 Out of Range
Low Magnesium
Trace Metals
Diet/Bad Fats
Mechanical
Gut Bacteria
This is not to be confused with "Puff"
PATIENT

Now Lets Drill Down:

1st: How are Fat Soluble Vitamins Transported
and
Who does the Transporting?

2nd: Size Matters with Regard to the "Trucks" (4 slides)

3rd: The "Readers Digest Version" Explanation of the Reversal of Heart Disease

4th: The "Painful Version" (trust me I will not dwell on it)

5th: A Practical Blue Collar Working Philosophy

6th: Everything you wanted to know about "K" but were afraid to ask (6 slides)

7th: Fetuin-A

8th: Suggested Tests

9th: Tips, Trick, Trivia, Terms, Trends, & Tantalizing Tidbit Travails (if we have time)

10th: A Plethora of References for your Reading Pleasure

The Delivery System of A, D, E, K, Ca, Q-10

CMr

Temple University Libraries, Urban Archives

K-1, MKs

CM

All

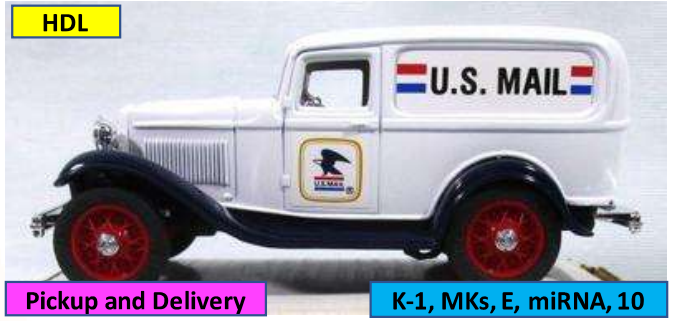
VLDL

K-1, MKs

DBP

Vit D

HDL



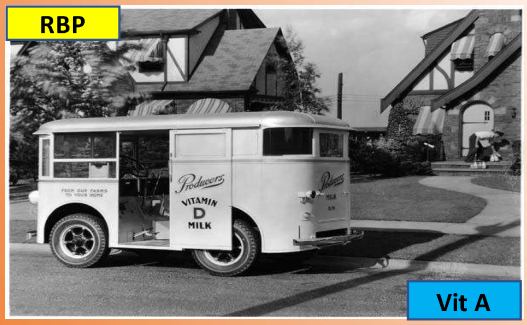
Pickup and Delivery

K-1, MKs, E, miRNA, 10

TRL

K-1, MKs

RBP



Vit A

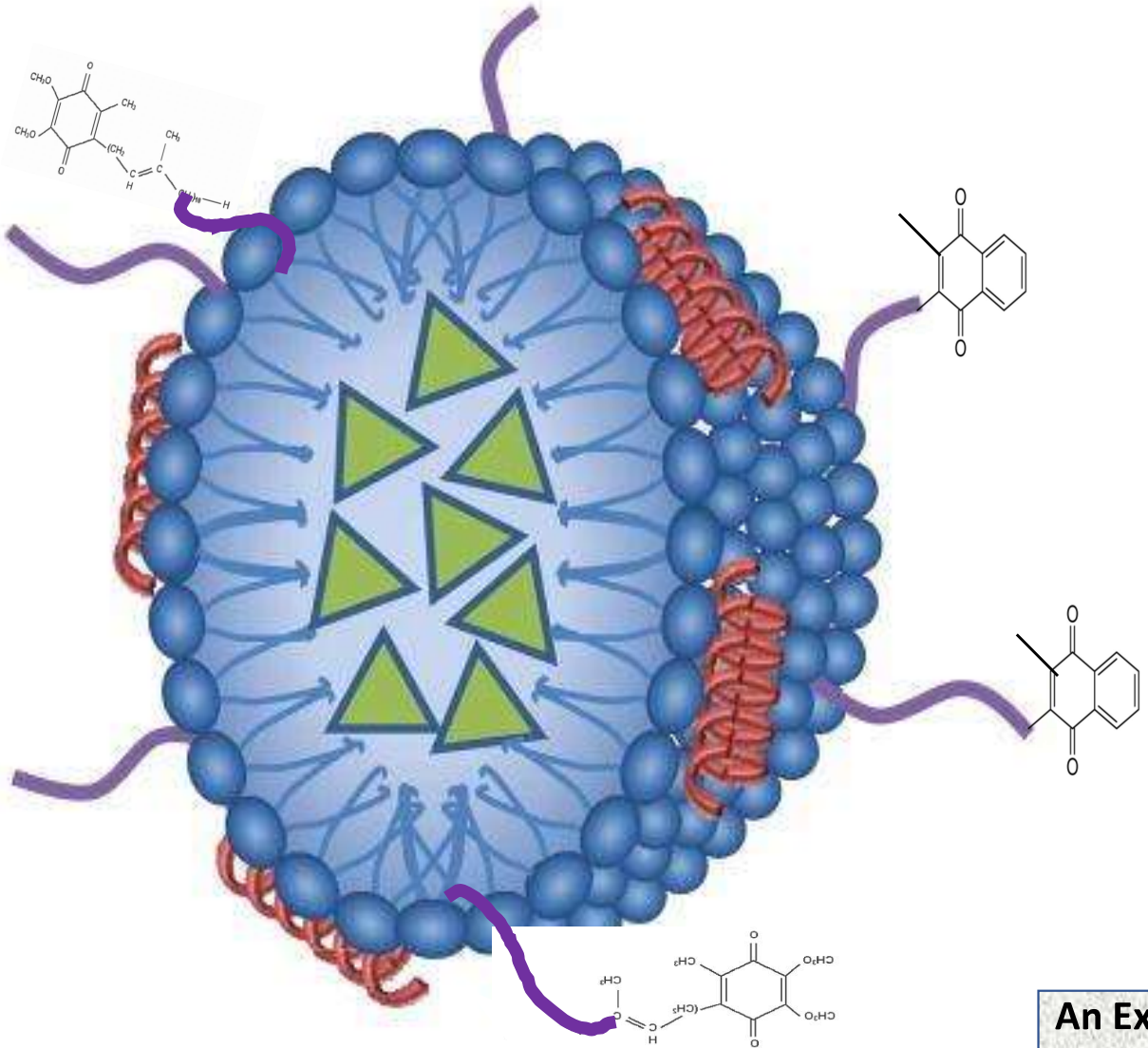
Fetuin-A

Pickup and Delivery

Calcium

LDL

K-1, MKs, E, 10



Hydrophobic cargo

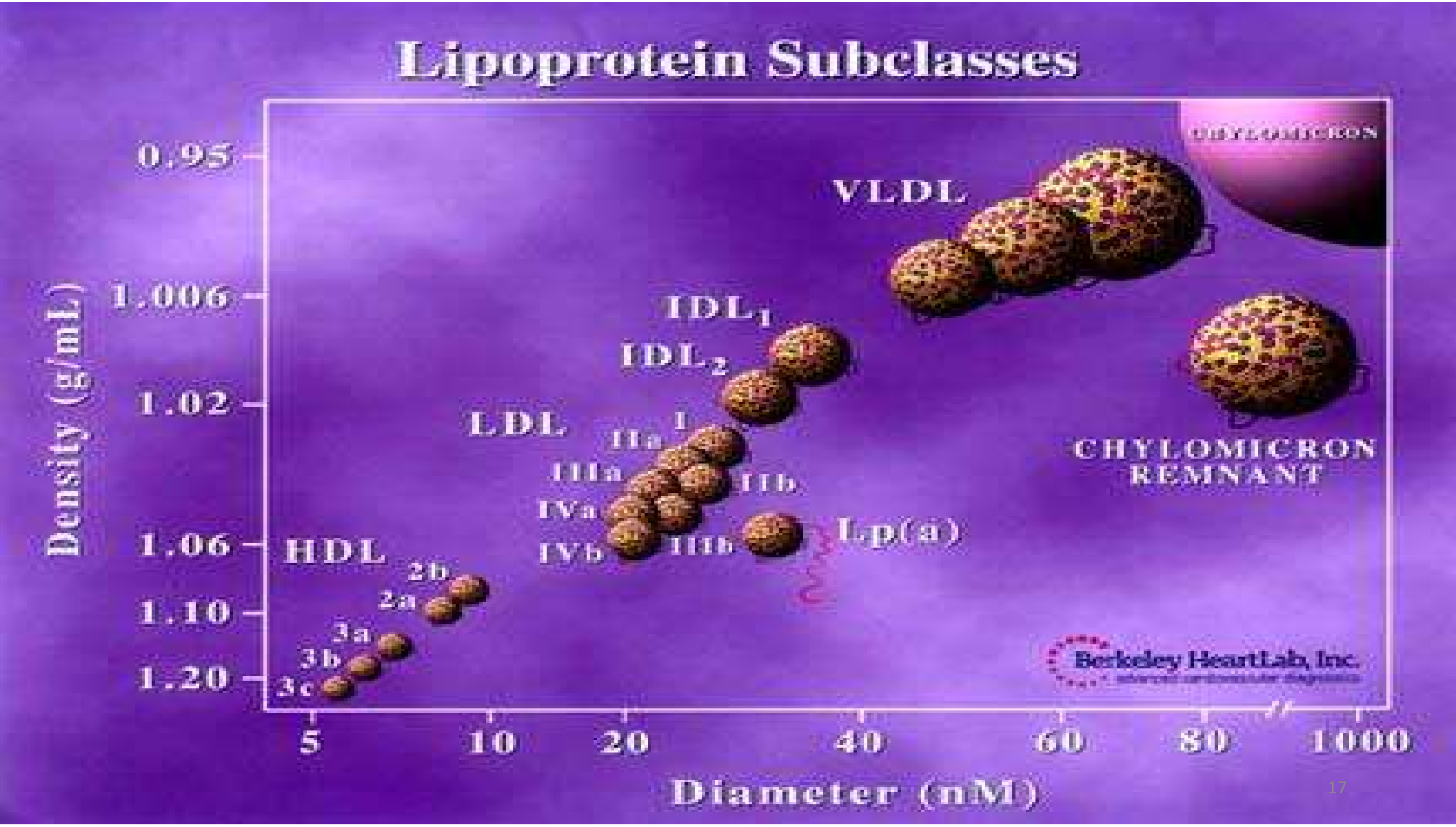
Hydrophilic cargo

Apolipoprotein/mimetic peptides

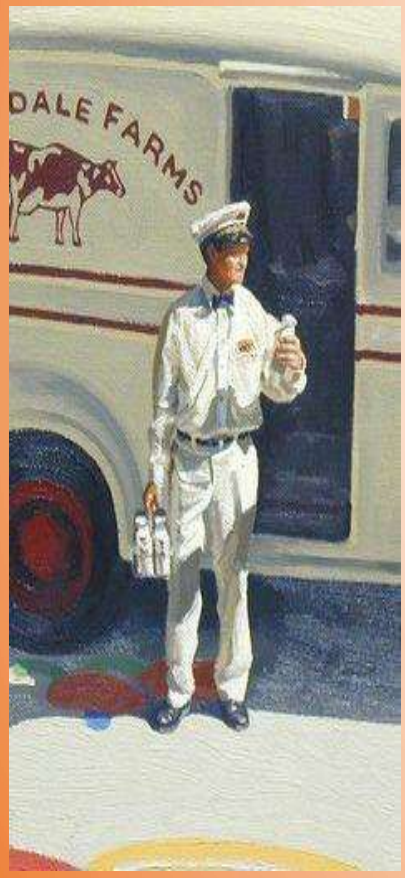
Phospholipid/Polymer

An Example of a Lipid with CoQ-10 and "K" Attached

"Its kinda-sorta-like-a-porcupine"


Lipoprotein Subclasses
0.95
1.006
1.02
1.06
1.10
1.20
Density (g/mL)
VLDL
IDL1
IDL2
LDL
I
IIa
IIIa
IIb
IVa
IVb
IIIb
Lp(a)
HDL
2b
2a
3a
3b
3c
CHYLOMICRON REMNANT
Berkeley HeartLab, Inc.
5
10
20
40
60
80
1000
Diameter (nM)

Size Matters As it Impacts Not Only How Much is Carried but How it is Carried Which IS The Surface Chemistry & Surface Orientation/Configuration Issue - - - - - Consider the Round Peg – Square Hole Analogy or Golf ball vs Beach ball



Particle	AVG Diameter nM	Lo	Hi	% Diff Lo to Hi Volume
CM	637	75	1200	409,600%
VLDL	55	30	80	1,896%
IDL	38	25	50	800%
LDL	23	18	28	376%
HDL	10	5	15	2,700%

Particle	AVG Diameter nM	Lo	Hi	% Diff Lo to Hi Surface Area
CM	637	75	1200	25,600%
VLDL	55	30	80	711%
IDL	38	25	50	400%
LDL	23	18	28	242%
HDL	10	5	15	900%

At the biophysiological level - - - the following appears to happen "Readers Digest Version"

The foam cell or macrophage or VSMC or the like gives off a warning chemical such as TNF-a and the like

These "fire alarm" chemicals are basically the body's version of "hey there is a problem here and I need help **NOW**" aka inflammation

Here is the internal fire department sans the Dalmatians:

First, is there is sufficient D in the system?

Second, are the LDL, VLDL, and HDL are properly coated with the appropriate K & E & Q-10 in sufficient amounts?

Third, did the Fetuin-A show up in sufficient amounts but not too much or too little?

Fourth, the Free T3, is it in the proper range - - - not too much or not too little?

Fifth, is there is sufficient Magnesium in the system?
(it "sloshes around in the serum")

Sixth, the APOE genotype does not express the "4" allele ?

Seventh, are the organic based antioxidants at the right level and available?

Eighth, is the calcium in the proper range - - - not too much or not too little?

The apparent sequence or "race to put out the fire":

ABCA-1/ABCG-1 is activated or up-regulated by FreeT3 (range of 3.5 to 5.0)

"D" riding on its carrier protein shows up due to the activation of ABCA-1/ABCG-1

the "D" in turn up-regulates the dp-ucMGP on the Macrophage/Foam Cell surface

Beta-HDL shows up with MK-7 attached and the MK-7 then carboxylates the MGP

Carboxylated MGP then allows for the HDL to start sucking out the lipids from the lipid core (reverse cholesterol transport) with help from CoQ-10 & miRNA

Carboxylated MGP caused by the presence of MK-7 on the LDL/HDL/VLDL particles then calls for and allows for Fetuin-A to go in and remove the Calcium from the area of the corrupted VSMC. If there is sufficient Magnesium present, it basically "loosens up" the Calcium associated with the hydroxyapatite thus, allowing for serum Calcium efflux (sorta like dissolving kidney stones) via Fetuin-A.

Fetuin-A now carrying the Ca, has two options to deal with the Ca. The first is dropping off the Calcium onto the bone or going back to the liver to be reprocessed (it has a half life of between 1 and 2 days - - similar to HDL).

Carboxylated MGP then allows for VLDL and LDL to go in and "kill" the Foam Cell/Macrophages Via K-1/MK-(x) - - -fo - - - autoschizis - - - - possibly "D/C" are also involved

Eventually, the "dead" VSMCs and the other cellular trash are reabsorbed over time.

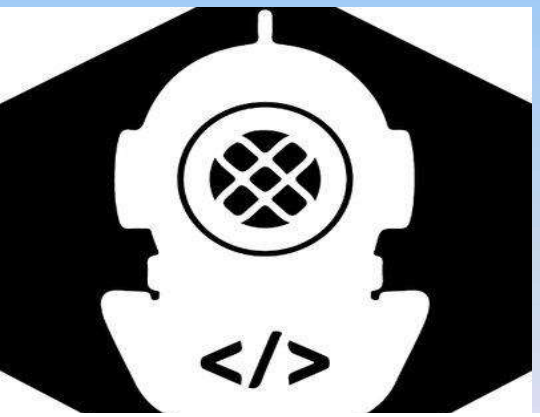
One hitch is your APOE status and the associated clearance rates of the VLDL, HDL, and LDL etc.

Now that the process has been clarified, lets do a deep dive

Triage Theory of Vitamin K

Vitamin K in its forms

Fetuin-A



Key Tests

The Sequence of Cardiac "fire fighting"

Fits the following philosophic model:

Measure it/Acknowledge it

Slow it Down

Stop it

Regress it

Heal it

Don't let it Happen Again

The "20 year fix" - - - - - Cardiac Reliability Maintenance Goal

Vitamin K, the Omni Vitamin - - - - "a bio-chemical passion play"

Vitamin K and Triage Theory

- Nature ensures that at suboptimal supply, vitamins and minerals are primarily used for functions required for short-term survival. The best example is the RDA for K-1 ONLY reflects clotting requirements. Also of note if one does not have enough K-1 but MK-7 is present or other MK's, the respective MK is substituted.
- K is not stored in any appreciable amount in any form as it appears to be too valuable all the time.
- Preferential distribution of phylloquinone et al to the liver is consistent with the triage theory proposed by McCann and Ames.
- Because carboxylation of the **most essential Gla** proteins is localized in the liver and that of the **less essential Gla** proteins in the extrahepatic tissues, a transport system has evolved ensuring preferential targeting to the liver to preserve coagulation when dietary vitamin K is inadequate. Only when at hepatic vitamin K sufficiency, particularly the long-chain menaquinones, is K transported to extra-hepatic tissues. **17 K dependent proteins that are known.**
- McCann and Ames concluded that long-term micronutrient insufficiencies are a risk factor for the development of a wide variety of age-related diseases, such as osteoporosis, cardiovascular disease (CVD), and cancer which are the result in part due to the incomplete or non-carboxylation of extra-hepatic Gla proteins aka Matrix Gla Proteins (MGP)
- **Note:** you cannot ever be fully Carboxylated
- The liver recycles "K" and has two pathways to do it, one could term it proactive sparing
- "MKs" in the intestine and liver appear to be made from other "anti-oxidants" aka precursors and that is signaling based much like "D" and Ca liberation from the gut.
- VK3 is remanufactured in the gut to other "Ks" **(lots of alternative pathways)**

Now, lets "drill down" in this "bio-chemical passion play"

Starting first with Vitamin K and its isoforms

K-1: Phylloquinone

MK(x): Menaquinone (4 to 14)

A. Cannot take too much, per the FDA, but **you have to take enough**

B. The half-life of K-1 one to two hours and MK-7 lasts two to three days.
MK-4 lasts a few hours to a half a day (much debate to MK-4 "life")
(Gut Bacteria? - - - folks forget that if you take a vitamin you are also feeding the gut bacteria too)

C. When taking a combination of both K's, lipid values will change dramatically especially if you are on a statin and then stabilize as LDL will increase then stabilize and HDL will increase and then stabilize. **(I did this on myself)**

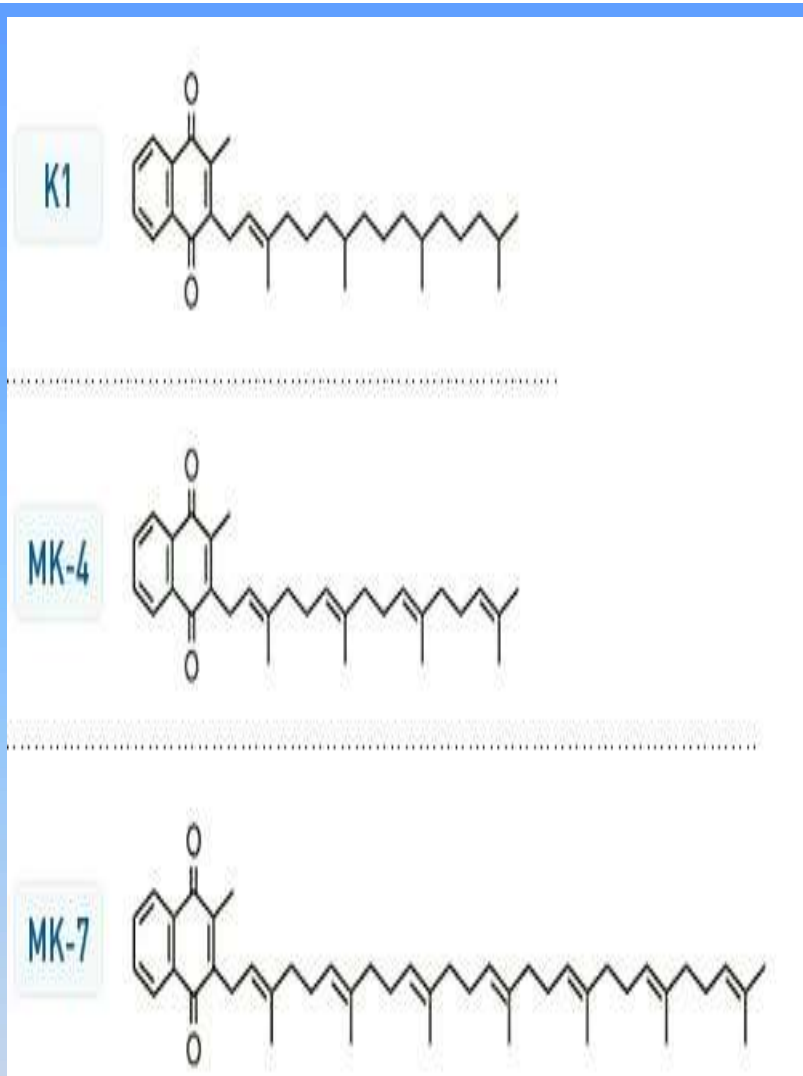
D. They are transported on the delivery trucks of the liver,
namely the VLDL, LDL, & Chylomicrons and Chylomicron ruminants
(note: HDL is the USPS truck of the liver and does double duty - - pickup and delivery)

E. K-1 deficiency is implicated in Alzheimer's and K-1 is carried on LDL (G. Ferland)

F. MK's in all their forms carboxylate K dependent proteins. Which is good.

G. MKs range from MK-4 to MK-14 (made or liberated in liver and/or gut and/or diet)

H. Therapeutic dose of K intake per day based on literature and conversations



The "bio-chemical passion play" Continued:

I. The Liver appears to make A in ratio to D and K so keep your Beta-Carotene levels sufficient

II. MK-7 Impacts Pulse Wave Velocity positively over time so make sure you have sufficient MK-7

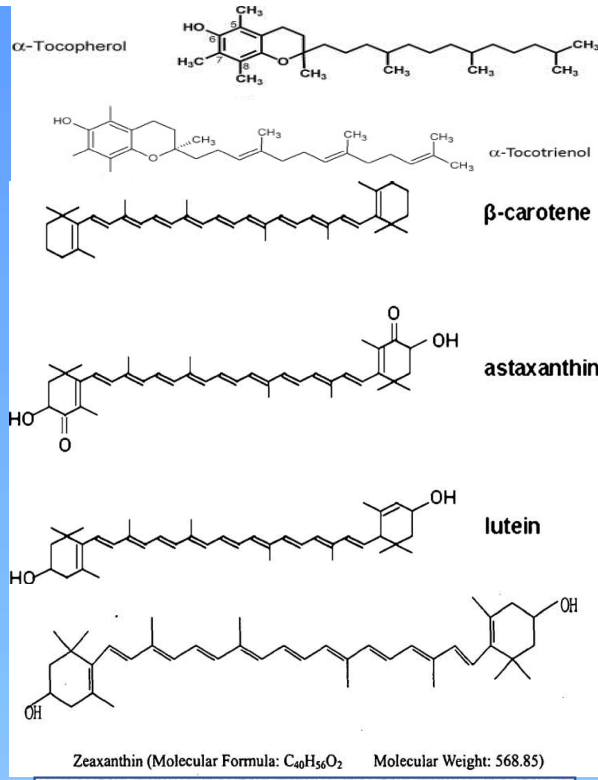
III. Abnormalities in the *MGP* gene have been linked with **Keutel syndrome** and **Pseudoxanthoma elasticum** (PXE) (absent or reduced MGP and Fetuin-A)

IV. Mice that lack *MGP* develop to term but die within two months as a result of arterial calcification which leads to blood-vessel rupture.

V. The isoprene units or phytyl units are hydrophobic thus stick onto or into the lipoprotein

VI. The term, Autoschizis: is a term derived from Greek meaning "self","to split". Autoschizis can be initiated via in vivo treatment with vitamin C (VC), synthetic vitamin K (VK3) or, better, a combination of both. The process that appears to what "kills" Macrophages &/or Foam Cells.

VII. Both phylloquinone and MKs may activate the steroid and xenobiotic receptor (SXR). SXR is a nuclear receptor involved in the transcriptional regulation of enzymes such as cytochrome P450 (in particular the CYP3A4 isoform).



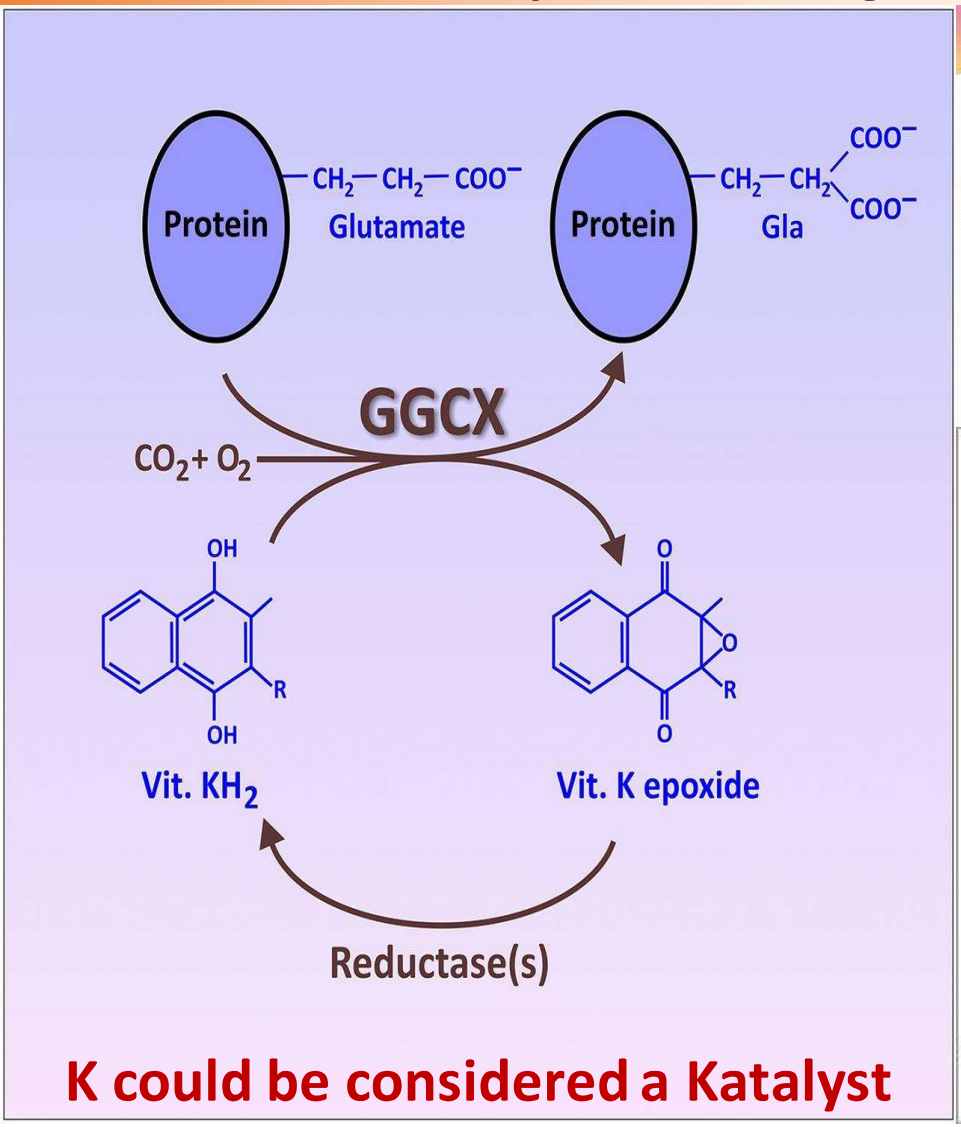
What do these look like?
"K" Pre-cursors for starters

VIII. Vascular calcification is an active ostogenic process thus driven in part due to the absence of "K" and the associated lack of carboxylation.

IX. Morphogen, BMP2, has an inhibitor, and its MGP. Warfarin inhibits MGP expression.

X. K-vitamins.com is the clearing house for peer reviewed literature by subject associated with K and its isoforms (specific "K" references included)

What is Carboxylation? Adding a COO to a protein via MK-7 and GGCX enzyme

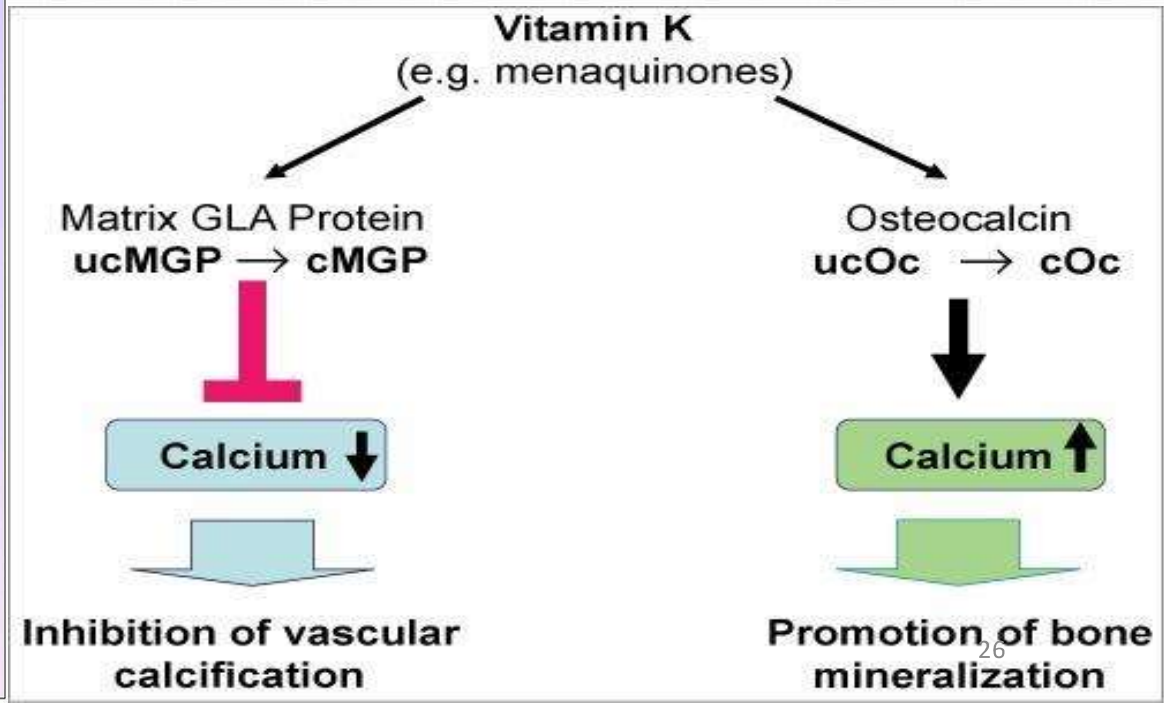


K could be considered a Katalyst

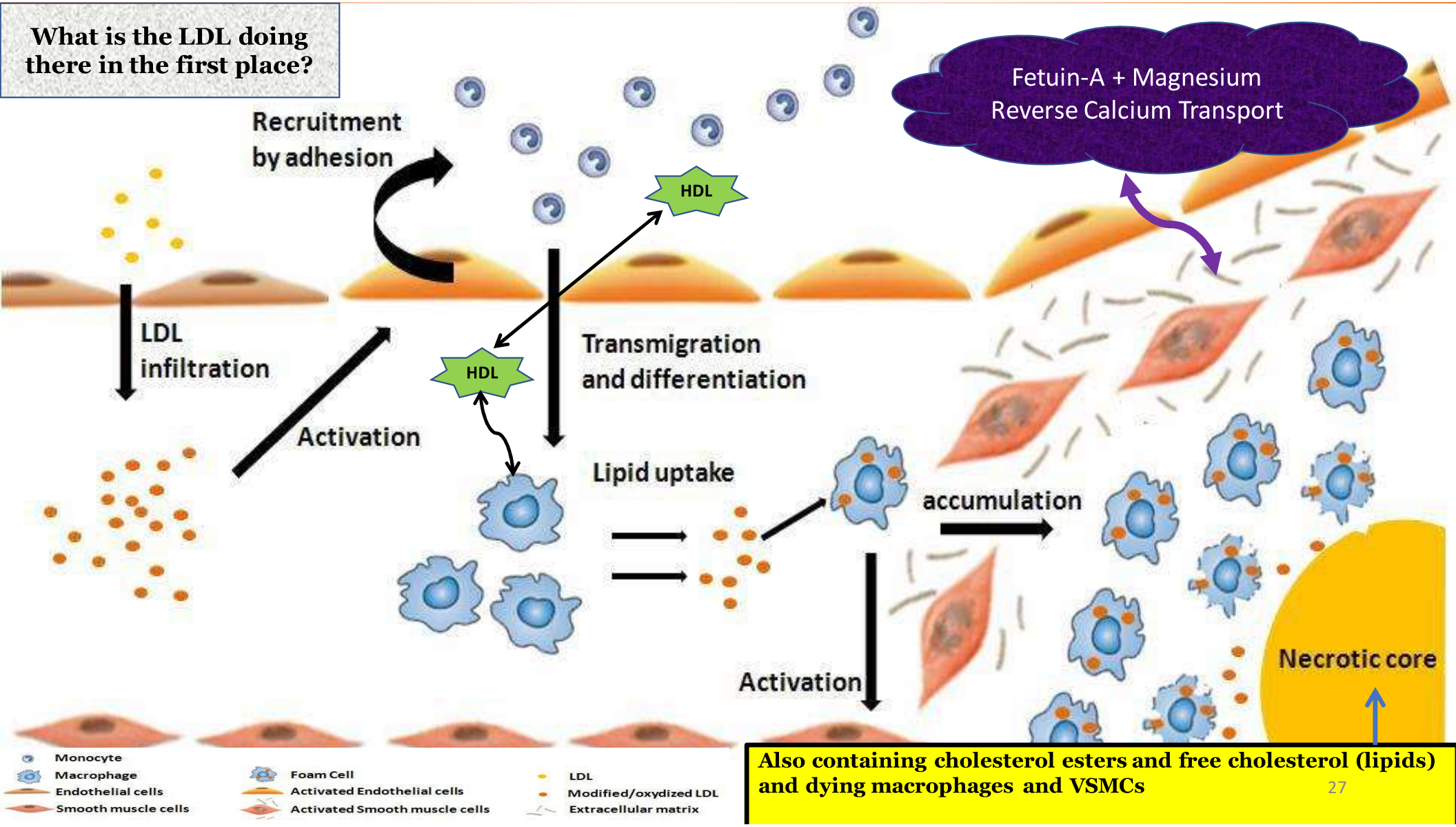
Vitamin K- dependent proteins

Major vitamin K-dependent proteins

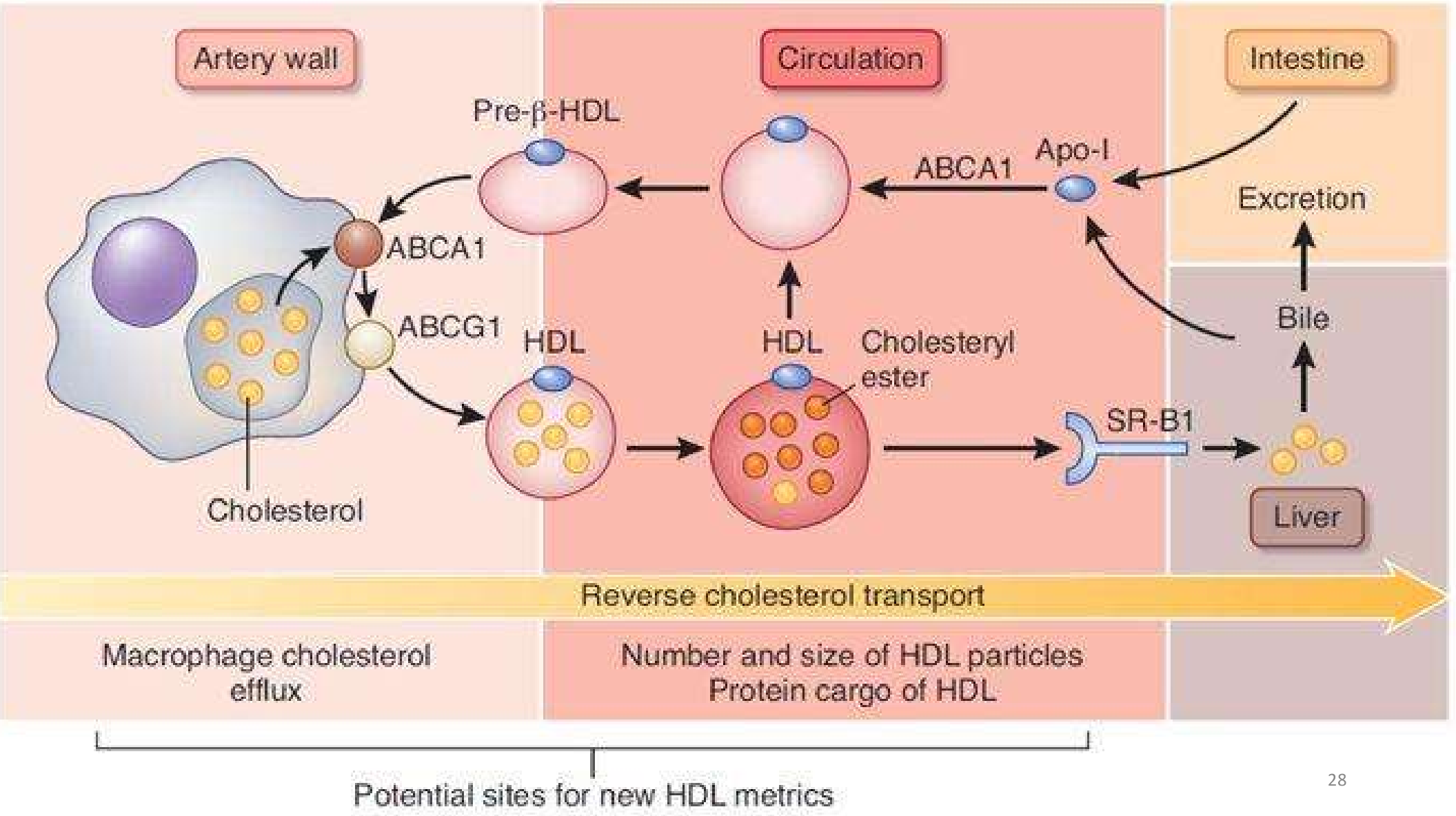
NAME	TISSUE	FUNCTION
Coagulation factors Anti-coagulation factors	Liver	Contribute to normal coagulation
Osteocalcin (OC)	Bone	Contribute to bone health
Matrix Gla Protein (MGP)	Aorta, heart valve	Inhibit calcification in artery
GAS6	Aorta, brain	Modulate cell growth



What is the LDL doing there in the first place?



Also containing cholesterol esters and free cholesterol (lipids) and dying macrophages and VSMCs


Artery wall
Circulation
Intestine
Pre-β-HDL
ABCA1
Apo-I
Excretion
ABCA1
ABCG1
HDL
HDL
Cholesteryl ester
Bile
SR-B1
Cholesterol
Liver
Reverse cholesterol transport
Macrophage cholesterol efflux
Number and size of HDL particles
Protein cargo of HDL
Potential sites for new HDL metrics

Fetuin-A

This Test Needs to be Routine!!!

Fetuin-A, which is also known as alpha 2-Heremans-Schmid glycoprotein (AHSG), is a multifunctional protein. In the fetus, fetuin-A is synthesized by multiple tissues. It is known as the Chaperone of Calcium

In adults, >95% of Fetuin-A is secreted by the liver. Fetuin-A inhibits insulin receptor tyrosine kinase and regulates bone remodeling and ectopic mineralization.

Increased levels of Fetuin-A have been linked to obesity and metabolic syndrome, chronic hyperglycemia and type 2 diabetes mellitus, non-alcoholic fatty liver disease, and the risk of albuminuria.

Fetuin-A is one of the hepatokines linked to obesity and cardiovascular diseases.

High serum Fetuin-A levels are associated with increased risks for myocardial infarction and ischemic stroke, carotid artery stiffness, and the severity of coronary artery disease.

In contrast, low Fetuin-A levels had been linked to an increased risks of coronary artery calcification and associated diseases.

1 to 2 day half life

Fetuin-A works in parallel with Vitamin D and Vitamin K and Magnesium. Neither of the three are required for Fetuin-A to be manufactured but upregulated MGP appears to activate Fetuin-A.

SUGGESTED TESTS RELATED TO THE PRESENTATION WITH RANGES & SUGGESTIONS:

PIVKA II (proteins induced in vitamin K absence) aka DCP: ng/ml 0.0–7.5 (ideal 0.00)

Uncarboxylated Osteocalcin: ng/ml 0.00 to 6.00 (lower is better – target less than 2.00)

Prothrombin Time: seconds 9.1 - 12.0 (suggest 11.0)

Vitamin D: ng/mL 10.0 - 100.0 (suggest over 60 but under 100)

Fetuin-A: mg/L 150 – 900 (suggestion 300 to 500 est) - - - NOT AVAILABLE!!!!!

CoQ-10: ug/mL 0.44 - 1.64 (suggest over 3.00)

APOE: Saliva Test, results provided as: 4/4,, 4/3,, 4/2,, 3/3,, 3/2,, 2/2

Vitamin K-1: (only useful for baseline) ng/mL 0.28 - 1.78 (when on K it will be saturated)

Red Blood Cell Magnesium: mg/dL 4.2 - 6.8 (suggest over 5.0)

CT Scan Once a Year: (ideal 0.00)

Red Blood Cell Selenium: mcg/L 120-300 (suggest mid-to-high range)

Vitamin C: mg/dL 0.2–2.0 (suggest 2.0 or greater or nominally 3 to 6 grams per day)

Free T3: pg/ml 3.5 to 5.0 (higher or lower is not good - - - mid range is ideal)

SUMMARY FOR THE PATIENT:

There is now hope based on objective evidence!

There is now a rational working definition

There is now a rational and easily understood working model

There is now a rational and easily understood working philosophy

But,
Each patient is slightly different so revel in the uniqueness because "one size don't fit all"

So

Test, Test, Test

&

Mellow out that Dragon

Tips, Tricks, Trends, Terms, Trivia,
&
Tantalizing Tidbit Travails

Role of Cholesterol

Cholesterol is used to:

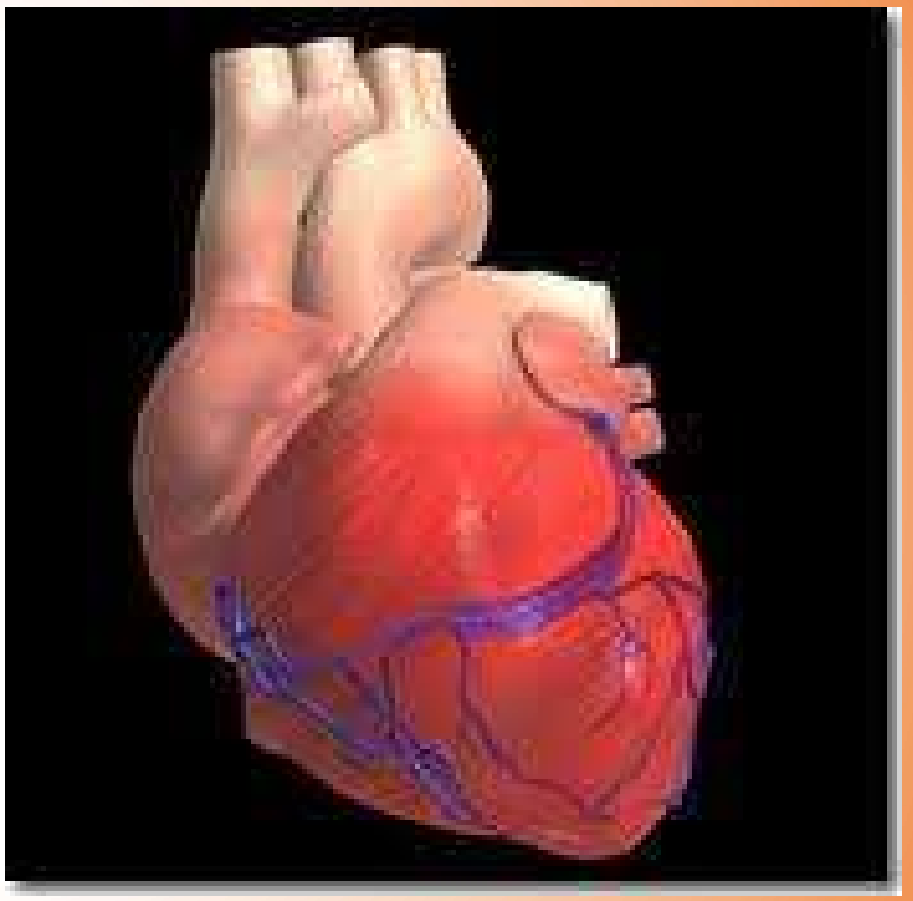
a.) Make cell membranes and nerve tissues

b.) Makes all the hormones starting with Pregnenolone

c.) Makes vitamin D

d.) OBTW vitamin D "talks" to the gut bacteria to release Calcium from food

e.) Produces bile, which helps digest fats



APOE

APOE isoforms differ in their rates of catabolism such that ε2 is catabolized more slowly than ε3 or ε4.

The increased rate of catabolism of apoE 4 leads to reduced availability of apoE to serve as a clearance protein, required for the clearance of cholesterol and toxic amyloid-beta (Aβ) oligomers.

Over 87% of centenarians are ε2/ε3 or ε3/ε3 among the majority of populations studied, including France, Japan, Spain, Italy, and Finland. While the ε3 allele is the most common, the prevalence among this age group is greater than the general population

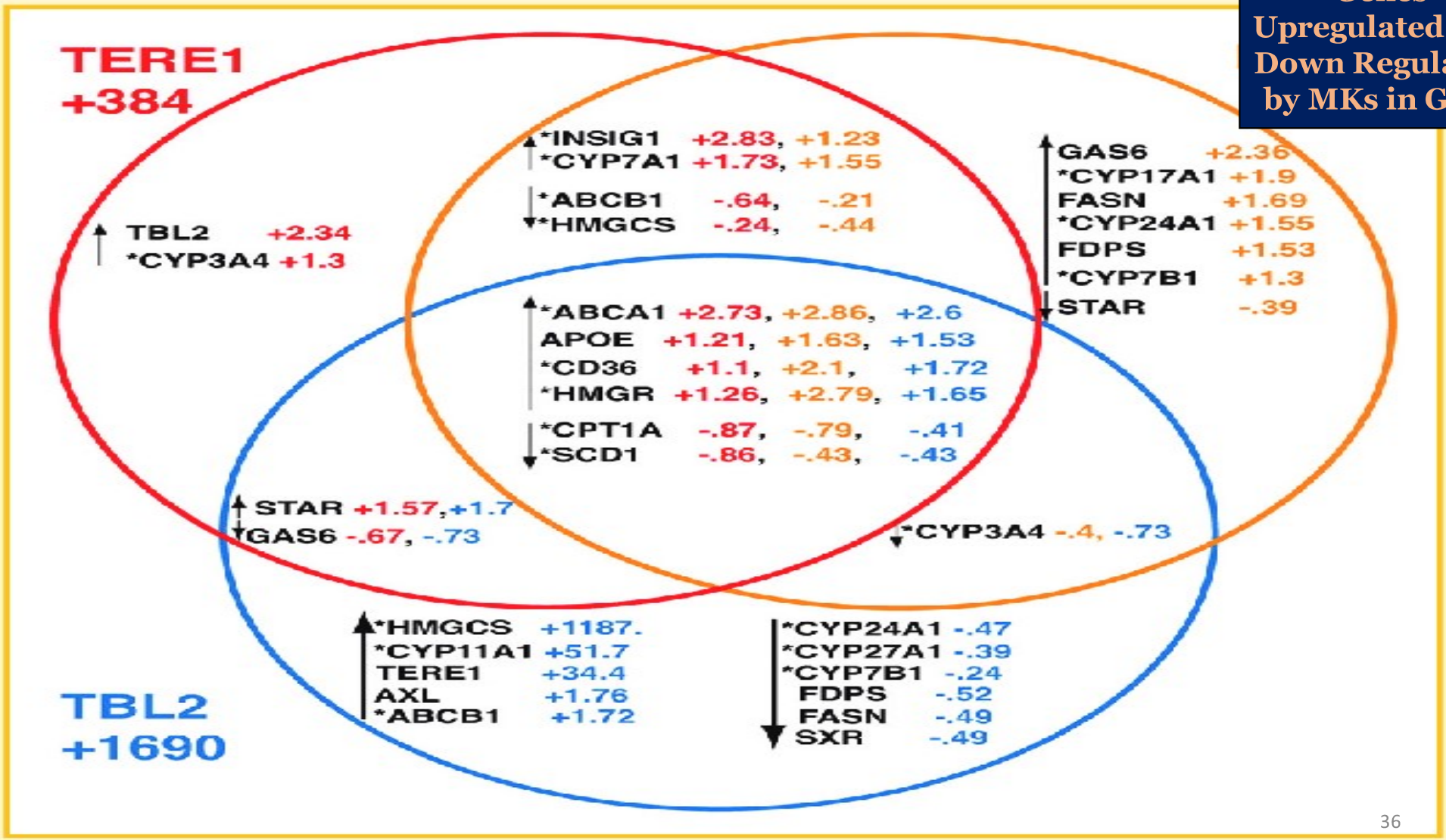
The 4/4 VLDL competed with human LDL for binding to the human LDL receptor slightly better than 3/3 VLDL, but the VLDL clearance rate in 4/4 mice was half that (read as took longer) than in 3/3 mice.

On an atherogenic diet, there was a trend toward greater atherosclerotic plaque size in 4/4 mice compared with 3/3 mice. These data, together with our earlier observations in wild-type and human *APOE*2*-replacement mice, demonstrate a direct and highly significant correlation between VLDL clearance rate and mean atherosclerotic plaque size.

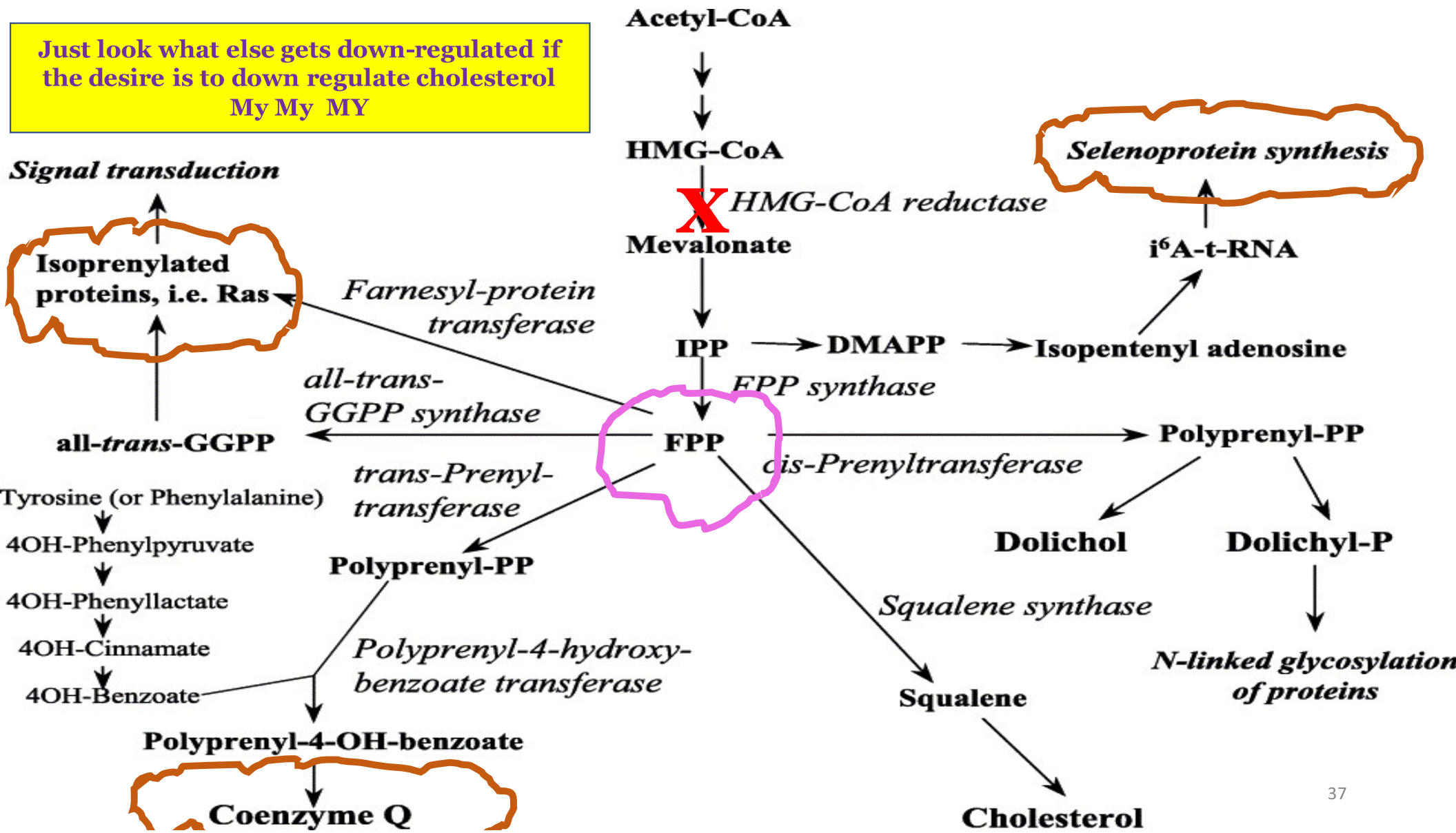
Therefore, differences solely in apo E protein structure are sufficient to cause alterations in VLDL residence time and atherosclerosis risk in mice.

The prevalence of APOE traits were ε2: 7.35%, ε3: 77.56%, and ε4: 15.09%

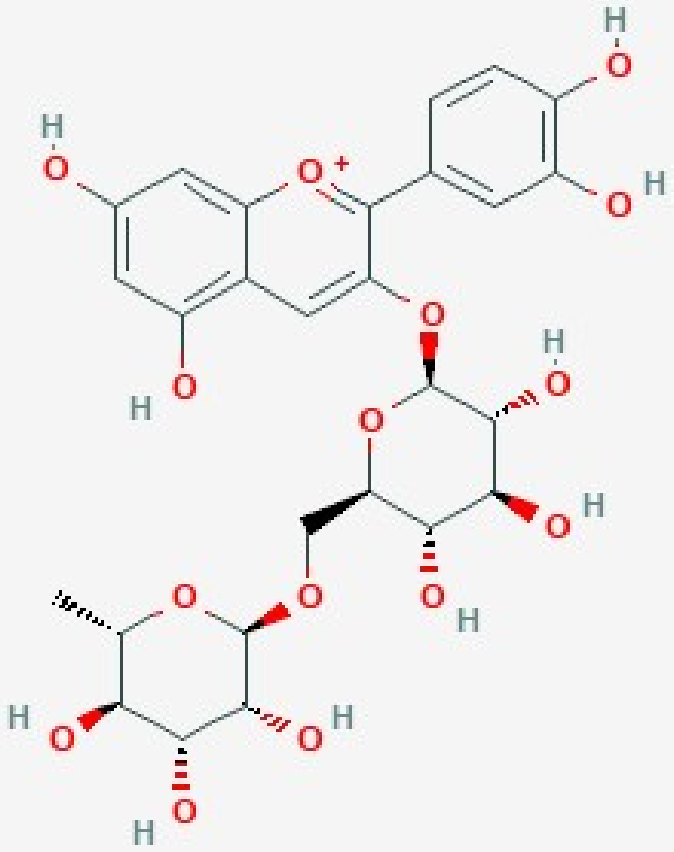
Genes Upregulated and Down Regulated by MKs in Gold

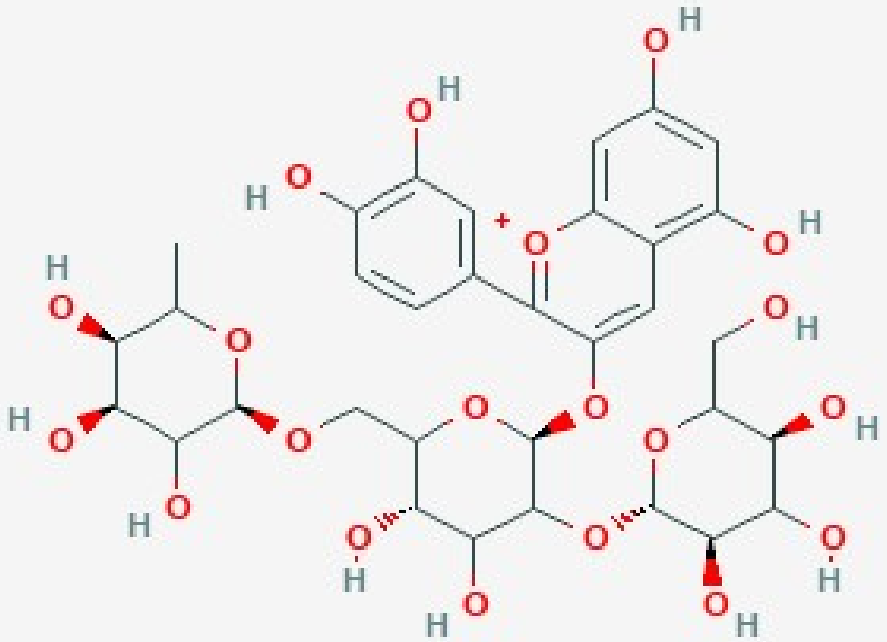


Just look what else gets down-regulated if the desire is to down regulate cholesterol
My My MY



Tart Red Cherry Typical Anti-Oxidants (look familiar?)





Top K-1 & K-2 Containing Foods - - - - 100 grams aka a “quarter-pounder”

K-1 Foods in mcg
dried basil –1714.5
dried sage – 1714.5
dried thyme – 1714.5
fresh parsley – 1640
dried coriander leaf – 1359.5
raw swiss chard – 830
raw dandelion greens – 778.4
cooked collard greens – 623.2
dried marjoram – 621.7
dried oregano – 621.7
cooked mustard greens – 592.7
raw cress – 541.9
cooked spinach – 540.7
cooked turnip greens – 518.9
cooked beet greens – 484
cooked kale – 418.5

K-2 Foods in mcg
natto – 939
soft cheese – 506
blue cheese – 440
goose liver – 369
hard cheese – 282
beef liver –106
pepperoni – 41.7 (sausage - tbd)
full-fat milk – 38.1
chicken meat –35.7
bacon – 35
turkey frankfurter – 31.2

Big Assumption(s) - - - - the “K” is Liberated Completely & Your Grocery Store Carries the “Stuff”