HEART DISEASE HAS BEEN THE LEADING CAUSE OF DEATH IN THE UNITED STATES **SINCE 1921**, AND STROKE HAS BEEN THE THIRD LEADING CAUSE SINCE 1938; TOGETHER THEY ACCOUNT FOR APPROXIMATELY 40% OF ALL DEATHS. (CDC AUG 6,1999)

NOW STROKE IS THE 5<sup>TH</sup> LEADING CAUSE OF DEATH HEART DISEASE IS STILL NUMBER 1

PREVALENCE OF CVD (COMPRISING CHD, HF, STROKE, AND HYPERTENSION) IN ADULTS ≥20 YEARS OF AGE IS 48.0% OVERALL (121.5 MILLION IN 2016) AND INCREASES WITH ADVANCING AGE IN BOTH MALES AND ON THE BASIS OF NHANES 2013 TO 2016 DATA, THE FEMALES

ACCORDING TO NHANES (NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY) 2015 TO 2016, 39.6% OF US ADULTS AND 18.5% OF YOUTHS WERE OBESE IN 2016, ≈17.6 MILLION (95% CI, 17.3–18.1 MILLION) DEATHS WERE ATTRIBUTED TO CVD GLOBALLY, WHICH AMOUNTED TO AN INCREASE OF 14.5% (95% CI, 12.1%-IN 2011 TO 2014, THE PREVALENCE OF HYPERTENSION AMONG US ADULTS WAS 45.6%

17.1%) FROM 2006

IN 2016, 2 744 248 RESIDENT DEATHS WERE REGISTERED IN THE UNITED STATES. TEN LEADING CAUSES ACCOUNTED FOR 74.1% OF ALL REGISTERED DEATHS. THE 10 LEADING CAUSES OF DEATH IN 2016 WERE THE SAME AS IN 2015; THESE INCLUDE HEART DISEASE (NO. 1), CANCER (NO. 2), UNINTENTIONAL INJURIES (NO. 3), CHRONIC LOWER RESPIRATORY DISEASES (NO. 4), STROKE (NO. 5), ALZHEIMER DISEASE (NO. 6), DM (NO. 7), INFLUENZA AND PNEUMONIA (NO. 8), KIDNEY DISEASE (NO. 9), AND SUICIDE (NO. 10)

AS MANY AS 50 PERCENT OF ALL CARDIAC DEATHS DUE TO DISEASE IN THE HEART'S VESSELS OCCUR IN INDIVIDUALS WITH NO PRIOR HISTORY OR SYMPTOMS OF HEART DISEASE. (2006)

### **HEART DISEASE IN THE UNITED STATES** (FROM CDC)

WOMEN, AND PEOPLE OF MOST RACIAL AND ETHNIC GROUPS HEART DISEASE IS THE LEADING CAUSE OF DEATH FOR MEN. IN THE UNITED STATES.

ONE PERSON DIES EVERY 34 SECONDS IN THE UNITED STATES FROM CARDIOVASCULAR DISEASE.

ABOUT 697,000 PEOPLE IN THE UNITED STATES DIED FROM HEART DISEASE IN 2020—THAT'S 1 IN EVERY 5 DEATHS.
HEART DISEASE COST THE UNITED STATES ABOUT \$229
BILLION EACH YEAR FROM 2017 TO 2018. THIS INCLUDES THE COST OF HEALTH CARE SERVICES, MEDICINES, AND LOST PRODUCTIVITY DUE TO DEATH.

#### HEART ATTACK

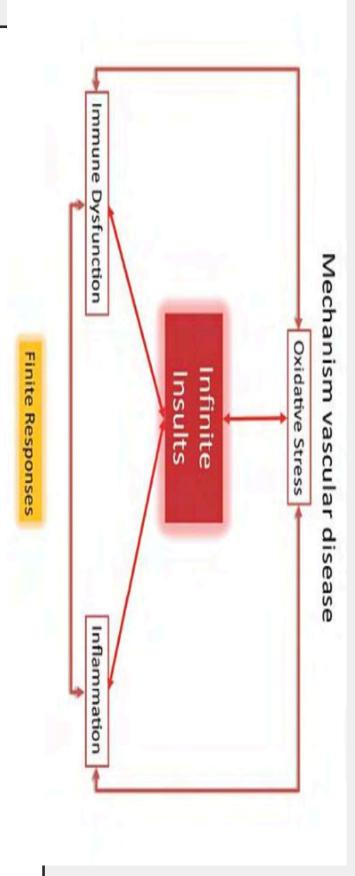
EVERY YEAR, ABOUT 805,000 PEOPLE IN THE UNITED IN THE UNITED STATES, SOMEONE HAS A HEART ATTACK EVERY 40 SECONDS. STATES HAVE A HEART ATTACK.2 OF THESE,

605,000 are a first heart attack

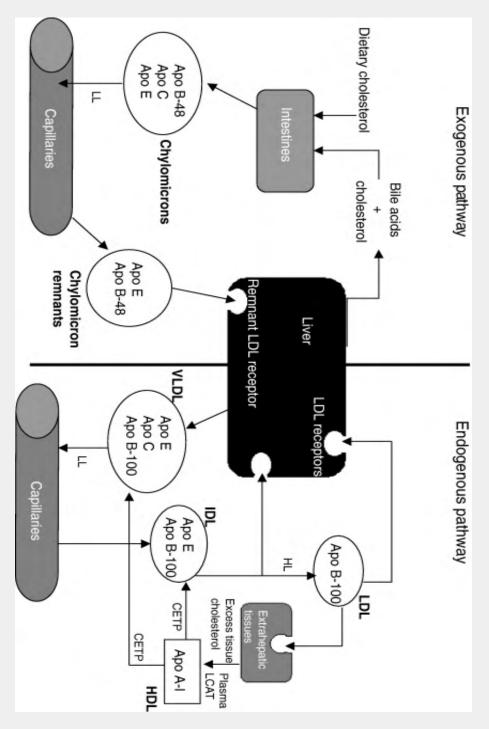
person is not aware of it. About 1 in 5 heart attacks are silent—the damage is done, but the 200,000 happen to people who have already had a heart attack

CYP4A11	Apo A2	Apo A1	ADR-B2	NOS3	GSHPx	CYP11B2	Corin		CYP1A2	MTHFR		ApoE	1q25	ACE i/d	COMT				<u>;</u> !	4a25		1	6p24.1		9p21 (GG/CC)	Gene Locus
rs1126742	rs5082	rs670	rs1042714	rs1799983	rs1050450 rs3918226 rs1549758	rs1799998	T555I and Q568P	rs762551	rs2472297	rs1801133 rs1801131	rs7412	rs429358	rs10911021	rs4646994	rs4680		rs10033464	rs10033464	rs2200733	rs2200733	rs499818	rs499818	rs169713	rs2383207	rs10757278	SNP
CTTT	СС	AA	GG		CC	⇉		AA CC AC	7	risk table available		risk table available	С	Del	AA GG		ℸ	GT	⊐ ։	1	D D	AG ?	CC	22	GG	Genotype Call
Higher hypertension risk	Obesity	Low HDL, CHD, MI	Hypertension and CHD	Ischemic heart disease	CHD, MI and hypertension	Hypertension with high urine and serum aldosterone levels. Poor response to medications with resistance	CHF with low Corin. Low ANP and BNP Increased salt sensitive hypertension.	metabolizers	Increased CHD, MI, hypertension, and arterial stiffness in slow	Increased risk for MI and CHD		E4/E4 with increased CHD and MI	Increased CHD in DM		Higher dopamine levels  Low Dopamine levels	Higher catecholamines. Hypertension, CHD and MI	1.4x AF and cardioembolic stroke	1.28x AF and cardioembolic stroke	1.5x increased risk for AF and IS	1 Ax Atrial Fibrillation and ischamic stroke			CHD and DVT		Heterozygote has 50 % increase risk for MI. Homozygote is 100% increase risk for MI. Also increase risk for DM, AAA	<u>Risk Association</u>
Amiloride		Niacin, Omega 3 FA, some statins.	DASH diet with ACEI or ARB	Nitric oxide precursors	Selenium, glutathione	Low sodium diet and SARA's	Avoid NaCL, increase nitric oxide with diet and arginine.		Avoid caffeine	Methylation treatment		CHD risk factor control	Control glucose. Consider Glutathione or precursors.	TLC to reduce HTN and cardiometabolic risk		Use of Vitamin E and ASA based on COMT							Farly identification, prevention and CHD risk factor control		Aggressive early detection prevention and CHD risk factor contro	Treatment Options

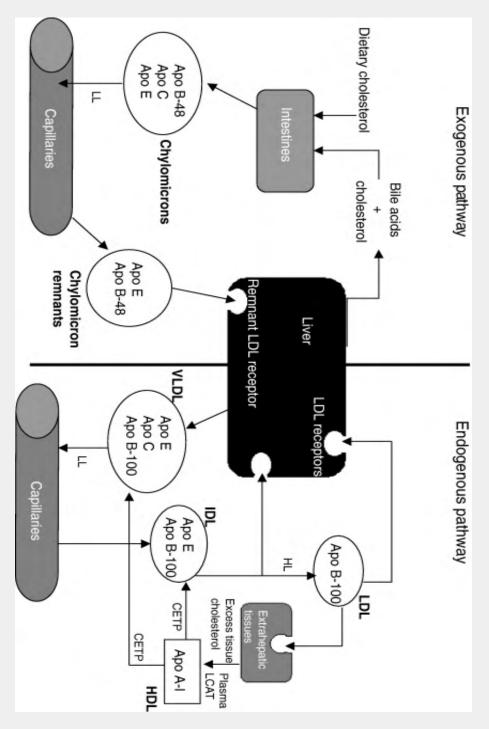
# WHAT TIES ALL THESE GENES TOGETHER?



# SO DO NOT THINK OF THE GENE WORKING THROUGH HYPERTENSION OR HEART DISEASE

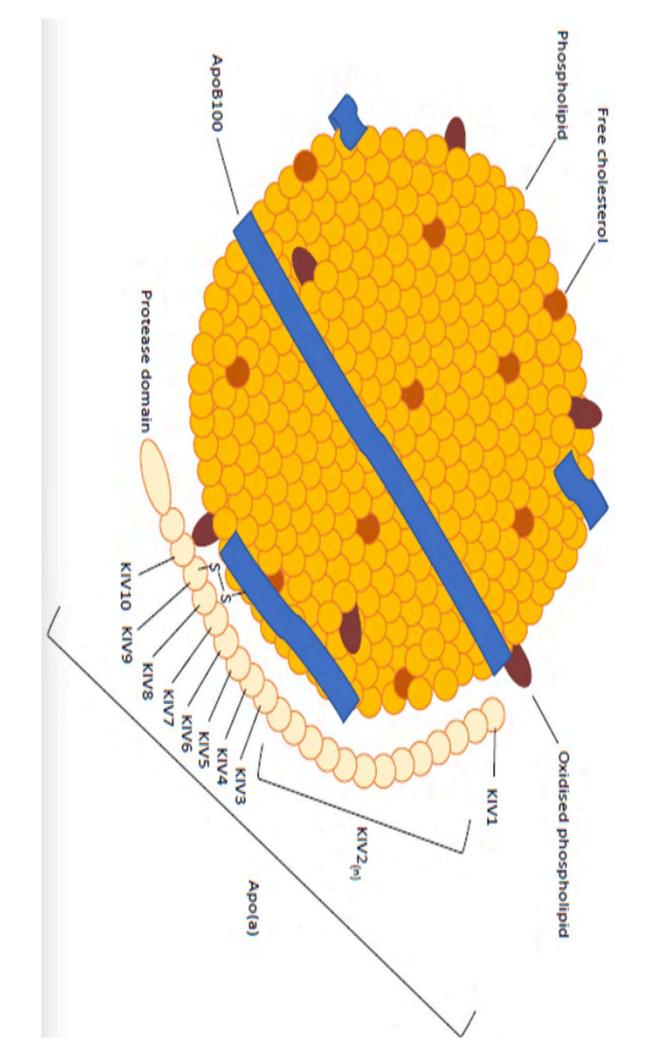


Journal of Internal Medicine, Volume: 255, Issue: 2, Pages: 188-205, First published: 26 January 2004, DOI: (10.1046/j.1365-2796.2003.01276.x)

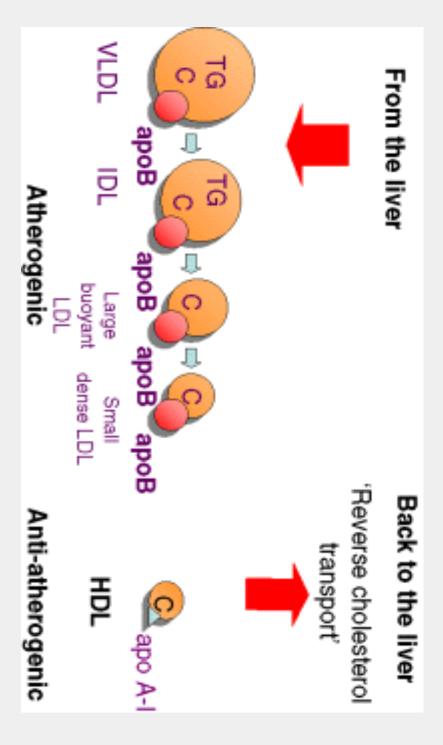


Journal of Internal Medicine, Volume: 255, Issue: 2, Pages: 188-205, First published: 26 January 2004, DOI: (10.1046/j.1365-2796.2003.01276.x)

Lipoprotein	Major apolipoprotein components
Chylomicron	B-48, C, E
VLDL	B-100, C, E
IDL	B-100, E
LDL	B-100
HDL	
Subfraction 2	A-I, A-II, C
Subfraction 3	A-II, A-I, C



targets for lipid-modifying therapy Apolipoprotein B and apolipoprotein A-I: risk indicators of coronary heart disease and



Journal of Internal Medicine, Volume: 255, Issue: 2, Pages: 188-205, First published: 26 January 2004, DOI: (10.1046/j.1365-2796.2003.01276.x)

### APOLIPOPROTEIN B

# **EUROPEAN CARDIOLOGY SOCIETY**

genetic, observational, and demonstrated beyond any doubt by development of ASCVD is apo-B-containing lipoproteins, in the The causal role of LDL-C, and other interventional studies.

# **EUROPEAN CARDIOLOGY SOCIETY**

relationship with LDL-C. Non-HDL-C levels contain, in lipoproteins, and is calculated as: total cholesterol encompasses all atherogenic (apo-B-containing) Non-high-density lipoprotein cholesterol (HDL-C) essence, the same information as a HDL-C and CV risk is at least as strong as the concentration. HDL-C = non-HDL-C. The relationship between nonmeasurement of apo-B plasma

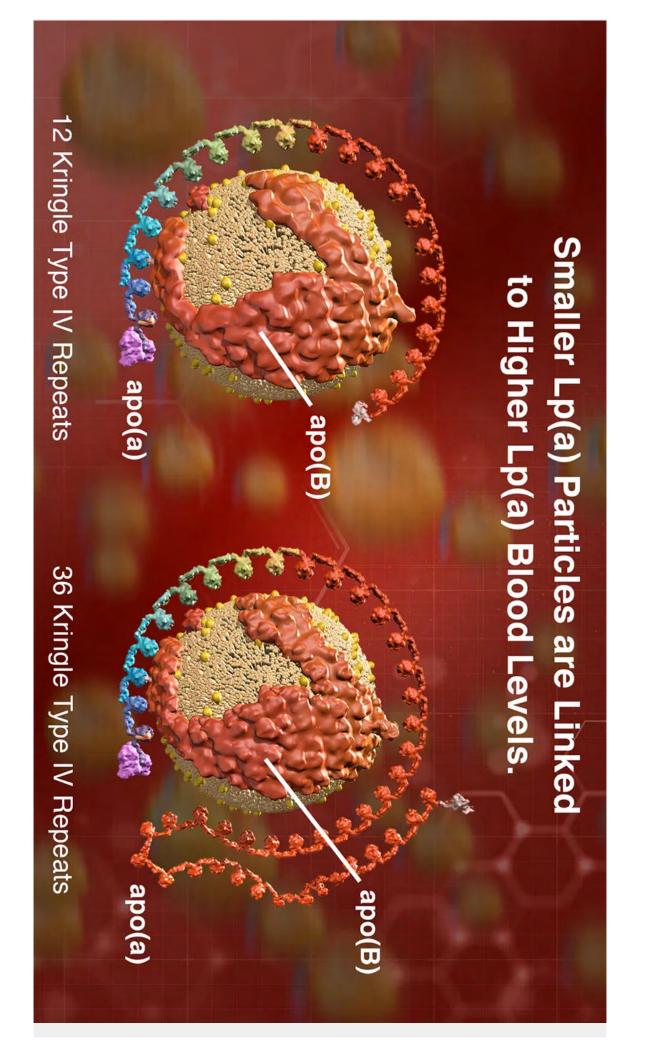
LIPOPROTEIN(A)

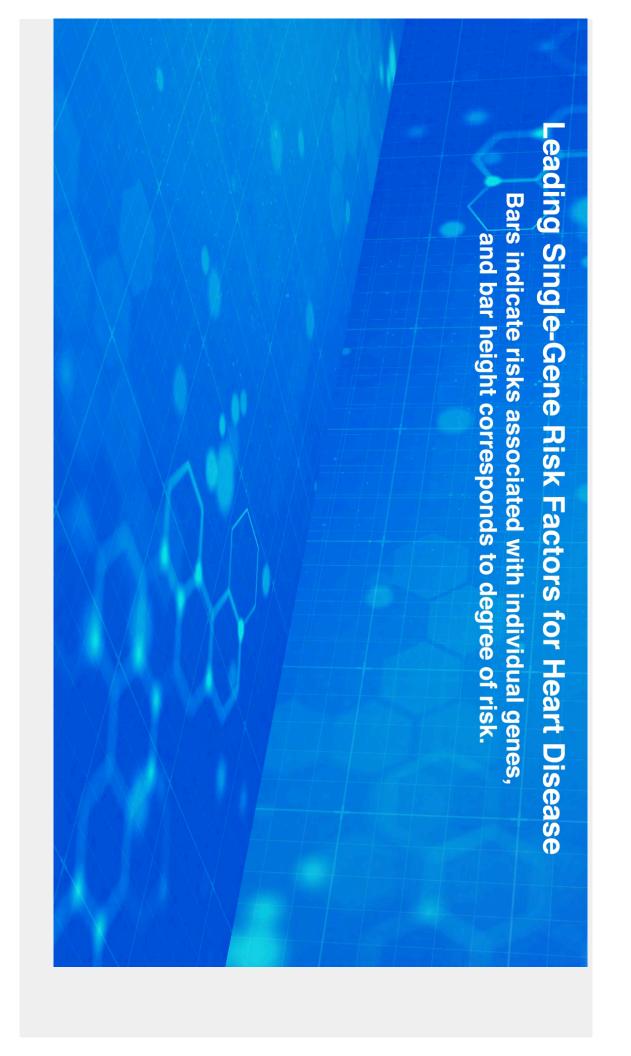
# SCIENCE & INNOVATION 02.28.2019

Why can heart attacks strike people who appear to be perfectly healthy? In some until its impact is felt. cases, the answer is a little-known risk, lipoprotein(a), which is rarely considered

#### ApoA XI 2 KIV KIV KIV KIV KIV KV FC CE LDL-like particle

### LIPOPROTEINA (a)

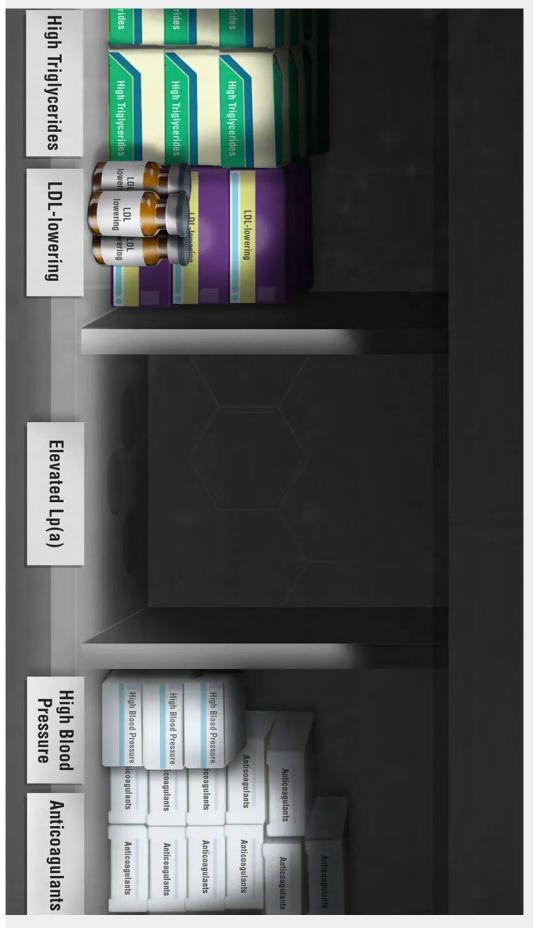








There are currently no approved medicines that directly target Lp(a).



Research on Lp(a) suggests it has added value in preventive medicine, and it is time for cardiologists and cardiovascular team members to consider using it routinely in their practice.

	Increased risk between highest and lowest Lp(a) concentrations	Association supported by Mendelian randomization study
Myocardial infarction	3- to 4- fold	Yes
Valvular aortic stenosis	3-fold	Yes
Coronary artery stenosis	5-fold	Yes
Carotid stenosis	1.7-fold	Yes
Ischemic stroke	1.6-fold	Yes
Femoral artery stenosis	1.6-fold	Yes
Heart failure*	1.5- to 2-fold	Yes
Cardiovascular mortality	1.5-fold	Yes
All-cause mortality	1.2-fold	Yes

tion front box menons notation attending a ferious Assistant Association 1 box 1 box

premature ASCVD, or ischemic stroke serial measurement of Lp(a) levels at Lp(a) levels remain stable throughout shows a link between elevated Lp(a) inflammation, there is not much role elevated Lp(a). However, given that history of first-degree relative with hypercholesterolemia (FH), family Interestingly, there may be a more genetically confirmed or clinically I herefore, it may be reasonble to or a parent/sibling found to have acute effect as current evidence and ischemic stroke in youth. measure Lp(a) in youth with one's life outside of acute suspected familial the present time

HOW DO YOU TREAT ELEVATED LP(A)?

Despite the observed associations between elevated Lp(a) and ASCVD, there has yet to be a randomized controlled trial to see if targeted lowering of Lp(a) improves clinical outcomes.

However, the Lp(a)-lowering effect of currently available therapies has been investigated.

HOW DO YOU TREAT ELEVATED LP(A)?

However more contemporary studies show that statin therapy in itself does affect Lp(a) levels; though importantly, those who continue to have high Lp(a) levels on a statin are at increased ASCVD risk even if LDL-C is improved.

#### HOW DO YOU TREAT ELEVATED LP(A)?

Hormone replacement therapy educes Lp(a), but its use is limited by the excess increase in adverse events

Niacin reduces Lp(a) 23% but did not improve ASCVD outcomes based on the AIM HIGH (Niacin Plus Statin to Prevent Vascular Events) and HPS2 THRIVE (Treatment of HDL to Reduce the Incidence of Vascular Events) studies. While tolerated by some, niacin is also associated with significant side effects. Furthermore, its efficacy is limited in those who may benefit the most (small isoform size and highest baseline Lp[a] levels).

#### LIPOPROTEIN (A)—WE KNOW SO MUCH YET STILL HAVE MUCH TO LEARN ...

APR2016
JOURNAL OF THE AMERICAN HEART
ASSOCIATION. 2016;5:E003597

effects by reducing LDL-C, total cholesterol, In addition to the discussion about the role agent to reduce residual risk of increasing of treating patients with high Lp(a) levels we are faced with the very great challenge countries commonly available in many European benefit with niacin administration as an trials did not show any cardiovascular cholesterol (HDL-C); however, the available by raising high-density lipoprotein triglycerides, and remnant cholesterol and addition exerts other potential beneficial to 40% in a dose-dependent manner and in cholesterol. Therefore, niacin is not high-density lipoprotein Niacin reduces Lp(a) levels by up to 30% therapeutic options to lower Lp(a) directly. Currently, the appropriate management of of Lp(a) as an important biomarker of CVD, high Lp(a) is not known and there are limited

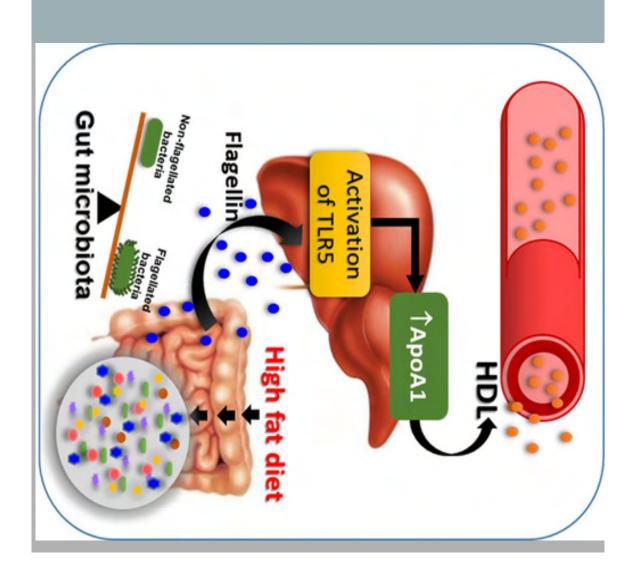
### **APOLIPOPROTEIN A1**

#### APO A1

GUT MICROBIOTAASSOCIATED ACTIVATION OF
TLR5 INDUCES
APOLIPOPROTEIN A1
PRODUCTION IN THE LIVER

Jensen H.C.Yiu, Kam-Suen Chan, Jamie Cheung, JinLi, Yan Liu, Yao Wang, William W.L. Fung, Jieling Cai, Samson W.M. Cheung, Bernhard Dorweiler, Eric Y.F. Wan, Patrick Tso, Aimin Xu, Connie W.Woo

Originally published21 Aug 2020https://doi.org/10.1161/CIRCRESAHA.120.317362Cir culation Research. 2020;127:1236–1252



#### APO A1

GUT MICROBIOTAASSOCIATED ACTIVATION OF
TLR5 INDUCES
APOLIPOPROTEIN A1
PRODUCTION IN THE LIVER

Jensen H.C. Yu, Kam-Suen Chan, Jamie Cheung, JinLi, Yan Liu, Yao Wang, William W.L. Fung, Jieling Cai, Samson W.M. Tso Aimin Xu. Connie W Woo

**Originally published**21 Aug 2020<u>https://doi.org/10.1161/CIRCRESAHA.120.317362</u>Cir culation Research. 2020;127:1236–1252

#### Conclusions:

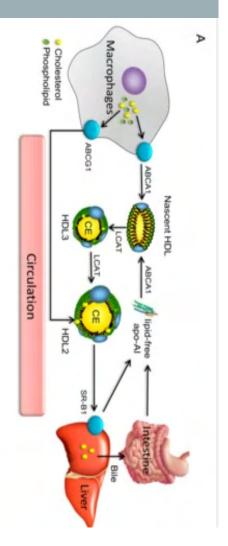
Our finding suggests that commensal flagellated bacteria in gut can facilitate ApoA1 and HDL-C productions in liver through activation of TLR5 in hepatocytes. Hepatic TLR5 may be a potential drug target to increase ApoA1.

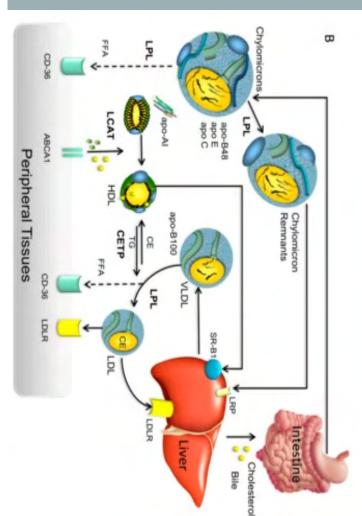
### ARTIFICIAL HIGH DENSITY LIPOPROTEIN NANOPARTICLES IN ARDIOVASCULAR RESEARCH

CARDIOVASCULAR RESEARCH
KARIN KORNMUELLER, IVAN VIDAKOVIC AND
RUTH PRASSL

RECEIVED: 14 JUNE 2019; ACCEPTED: 1 AUGUST 2019; PUBLISHED: 2 AUGUST 2019

Figure 1. Schematic diagram of high density lipoprotein (HDL) metabolism in the circulatory system. (A) apolipoprotein AI (apoA-I) is synthesized in the liver and intestine in lipid free form. apo-AI becomes rapidly lipidated with phospholipids and cholesterol via the hepatocyte ATP-binding cassette AI (ABCAI) transporter to form discoidal nascent HDL. In peripheral tissues nascent HDL particles take up free cholesterol via the macrophage ABCAI and ABCGI transporters. The free cholesterol becomes esterified by lecithin-cholesterol acyltransferase (LCAT) to form cholesteryl esters (CE). Mature HDL3 particles are formed that can be converted to HDL2. Further, HDL2 can be either taken up by the liver via SR-BI or might be modified by endothelial or hepatic lipases. (B) Overview of lipoprotein mediated lipid transport mechanisms.





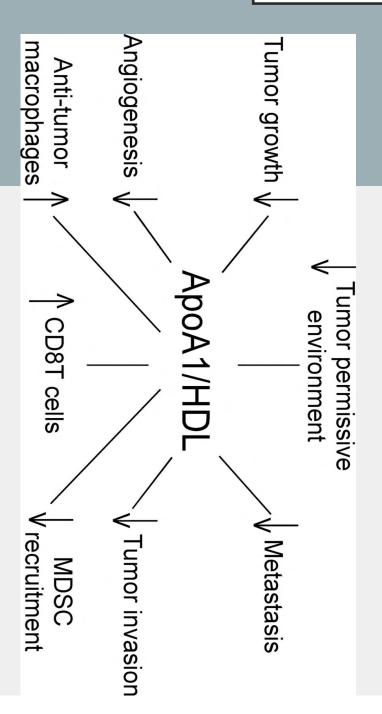
CARDIOPROTECTIVE
PROTEIN
APOLIPOPROTEIN A1
PROMOTES POTENT
ANTI-TUMORIGENIC
EFFECTS\* •

Maryam Zamanian-Daryoush, Daniel Lindner, Thomas C. Tallant, Zeneng Wang, Jennifer Buffa, Elizabeth Klipfell, Yvonne Parker, Denise Hatala, Patricia Parsons-Wingerter, Pat Rayman, Mohamed Sharif S. Yusufishaq, Edward A. Fisher, Jonathan D. Smith, Jim Finke, Joseph A. DiDonato, Stanley L. Hazen

Journal of Biological Chemistry

Volume 288 Issue 29 Pages 21237-21252 (July 2013)

DOI: 10.1074/jbc.M113.468967





## SUMMARY OF OTHER MARKERS

#### <u>PLAC</u> (LP-PLA2)

a vascular-specific inflammatory marker critical in the formation of rupture-prone plaque. Lp-The PLAC® Test for Lp-PLA2 activity measures the function of Lp-PLA2 in the artery wall events. A PLAC test may sometimes be used along with an hs-CRP test to evaluate a PLA2 Activity, the greater the risk of fatal and non-fatal coronary heart disease (CHD) intlammatory condition, such as arthritis. that can cause general inflammation, so it may be used when someone has an person's level of underlying inflammation associated with Cardiovascular Disease (CVD) with a prognostic value independent of standard lipid profile testing. The greater the Lp-PLA2 activity is a novel risk predictor in people with no prior history of cardiovascular events risk. However, unlike hs-CRP, the PLAC test is not affected by conditions other than CVD

#### HOMOCYSTEINE

Homocysteine may be ordered as part of a screen for people at deficiency, even before those tests show abnormal results. obesity. It may be an early indicator of Vitamin B12 and Folate who has a family history of coronary artery disease but no other known risk factors such as smoking, high blood pressure, or high risk for heart attack or stroke. It may be useful for someone

#### 1S-CRP

sugar. Excessive inflammation has been linked to heart disease sensitivity C-reactive protein) test. Inflammation is a way for the C-reactive protein (CRP) is a protein that the liver makes when can be caused by smoking, high blood pressure, and high blood body to protect itself from injuries or infections, and inflammation inflammation, and can be measured with an hs-CRP (highthere is inflammation in the body. It's also called a marker of

#### OXIDIZED LDL

also play a role in increasing the amount of triglycerides oxidation of LDL, creating a vicious cycle. deposited by the body. In turn, fat tissue can enhance the arteries, also known as atherosclerosis. Oxidized LDL may that has been modified by oxidation. Oxidized LDL triggers the body produces, as well as increasing the amount of fat inflammation leading to the formation of plaque in the Oxidized LDL is LDL cholesterol (the "bad" cholesterol)

#### MPO

Myeloperoxidase (MPO) enzyme is found in neutrophil primary granules and monocyte lysosomes. MPO catalyzes the enzyme found in leukocytes. undergoes posttranslational modification to produce the active hypochlorous acid. MPO is encoded by a single gene that conversion of hydrogen peroxide to hypochlorite and

#### NT-PROBNP

(MYOCARDIAL STRESS)

NT-proBNP is primarily secreted from the cardiac ventricular presence of an underlying cardiac disorder. diagnostic and prognostic tool as elevated levels may indicate the myocytes in response to cardiac stress. NT-proBNP is a useful

### OMEGA-3 & OMEGA-6

Omega-3 fatty acids are polyunsaturated fatty acids (PUFAs) with a double bond associated with a decreased risk of coronary heart disease omega-3 fatty acids, omega-6 fatty acids (eg, arachidonic acid [AA]) and their consumption of omega-6 fatty acids in place of saturated fats and trans fats is eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). The American metabolites are more proinflammatory than anti-inflammatory. Increased of omega-3 fatty acids involved in human physiology are α-linolenic acid (ALA), intake of omega-3 fatty acids to reduce cardiovascular disease risk. In contrast to Heart Association and the European Society for Cardiology recommend dietary (C=C) at the third carbon atom from the end of the carbon chain. The three types

#### **TMAO**

red meat, egg yolk and full-fat dairy products. When consumed, these nutrients are as lecithin), choline, and L-carnitine are abundant in animal-derived products such as roles in host defense, immunity, and nutrient processing and absorption. This diverse Gut microbes live symbiotically within the human digestive tract and play important processes involved in the development of atherosclerosis. converted into TMAO which has been shown to regulate various physiological processed by gut bacteria resulting in the release of various metabolites including TMA exposures to various food sources. Nutrients such as phosphatidylcholine (also known community is unique to each person and influenced by both acute and chronic dietary (trimethylamine) into the blood. TMA is then transported to the liver where it is

#### F<sub>2</sub>-ISOPROSTANES

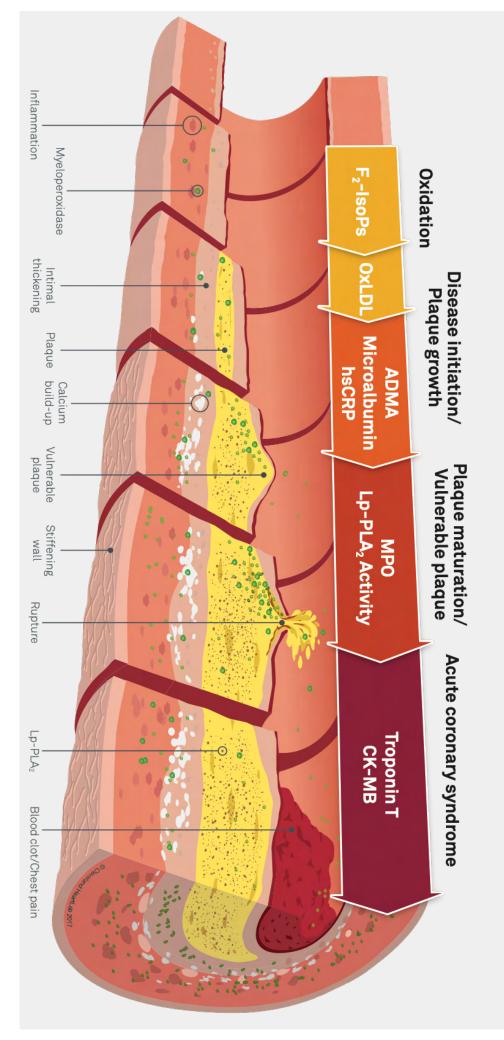
F<sub>2</sub>-IsoPs are prostaglandin-like compounds formed from the free radicalplatelet activation resulting in thrombus formation. vasoconstrictors via thromboxane formation in the endothelium, and promote effects associated with inflammation and therefore may mediate chronic disease initiation and progression. Additionally, F<sub>2</sub>-IsoPs may also act as potent mediated oxidation of arachidonic acid, and are the 'gold standard' for measuring oxidative stress in the body. F<sub>2</sub>-IsoPs also have potent biological

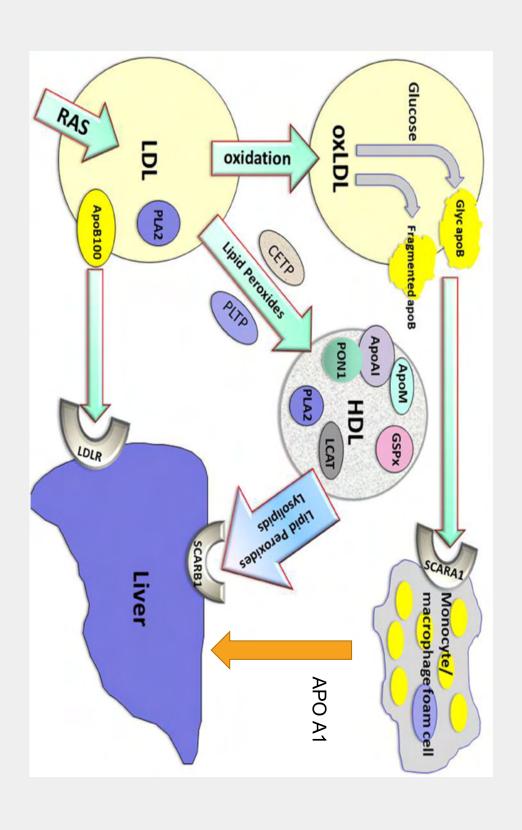
## MYELOPEROXIDASE (MPO)

artery wall including fissures, erosions or a degrading collagen cap, leads to MPO accumulates. MPO mediates the vascular inflammation that propagates plaque activity from the luminal aspect of the arterial wall. Briefly, when the artery wall is MPO is a white blood cell-derived inflammatory enzyme and measures disease formation and activates protease cascades that are linked to plaque vulnerability. damaged, or inflamed, MPO is released by invading macrophages where it release in the bloodstream. White blood cell activation in the bloodstream, in response to luminal injury of the

# Inflammatory Biomarkers and their Association with Atherosclerosis

measured to help evaluate a patient's risk for heart disease and cardiovascular events. Atherosclerosis is associated with specific inflammatory biomarkers, which can be





BLOOD PRESSURE

#### HYPERTENSION . 2020 FEB;75(2):285-292. HIGH BLOOD PRESSURE AND CARDIOVASCULAR

DISEASE

- Fragmented investigation has masked the overall picture for causes of cardiovascular disease (CVD).
- Among the risk factors for CVD, high blood pressure (BP) is associated with the strongest evidence for causation and it has a high prevalence of exposure. Biologically, normal levels of BP are considerably lower than what has typically been characterized as normal in research and clinical practice.
- We propose that CVD is primarily caused by a right-sided shift in the population distribution of BP. Our view that BP is the predominant risk factor for CVD is based on conceptual postulates that have been tested in observational investigations and clinical trials.
- Large cohort studies have demonstrated that high BP is an important risk factor for heart failure, atrial fibrillation, chronic kidney disease, heart valve diseases, aortic syndromes, and dementia, in addition to coronary heart disease and stroke.

### LANCET 2008 MAY 3;371(9623) GLOBAL BURDEN OF BLOOD-PRESSURERELATED DISEASE, 2001

About 54% of stroke and 47% of ischemic heart disease worldwide were attributable to high blood pressure.

### ASSOCIATION OF NORMAL SYSTOLIC BLOOD PRESSURE LEVEL WITH CARDIOVASCULAR DISEASE IN THE ABSENCE OF RISK FACTORS

SEAMUS P. WHELTON, MD, MPH1; JOHN
W. MCEVOY, MB, BCH,
MHS1,2; LESLEE SHAW, PHD3; ET AL

JAMA CARDIOL. 2020;5(9):1011-1018. DOI:10.1001/JAMACARDIO.2020.17 31

- In this cohort study including 1457
  participants without atherosclerotic
  cardiovascular disease, beginning with a
  systolic blood pressure level of 90 mm
  Hg, there was a stepwise increase in the
  prevalence of traditional atherosclerotic
  cardiovascular disease risk factors,
  coronary artery calcium, and the risk of
  atherosclerotic cardiovascular disease.
- For every 10-mm Hg increase in systolic blood pressure, there was a 53% higher risk for atherosclerotic cardiovascular disease.

## CAFFEINE (AND ITS CLEARANCE)

#### MPLICATIONS FOR RISK, CAFFEINE AND STRESS: MANAGEMENT OF ASSESSMENT, AND HYPERTENSION

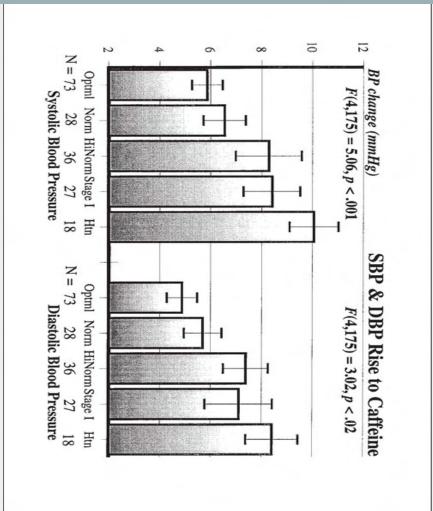
DEC; 3(6): 354–382.

TERRY R. HARTLEY, PHD, 1 WILLIAM R.
LOVALLO, PHD, 1 THOMAS L. WHITSETT,

MD, 1 BONG HEE SUNG, PHD, 1 AND MICHAEL

F. WILSON, MD 1 CLIN HYPERTENS (GREENWICH). 2001 NOV-

150–175-lb man) in five groups stratified by risk for hypertension (Htn) according to Joint National Committee (JNC) VI Scriteria. There were 73 with optimal (Optml) Bps (<120/80 mm Hg), 28 with normal (Norm) Bps (120/80–129/84 mm Hg), 36 with high-normal (HiNorm) Bps (130/85–139/89 mm Hg), 27 with stage 1 hypertension (140/90–159/99 mm Hg), and 18 who had been Systolic and diastolic blood pressure (SBP/DBP) increases on oral caffeine intake (3.3 mg/kg, equivalent to about 2.5–3 cups of coffee in a medicated for hypertension and had been vithdrawn from medication for 2–4 weeks.



### THE INFLUENCE OF CYP1A2 GENOTYPE IN THE BLOOD PRESSURE RESPONSE TO CAFFEINE INGESTION IS AFFECTED BY PHYSICAL ACTIVITY STATUS AND CAFFEINE CONSUMPTION LEVEL

VASCULAR PHARMACOLOGY VOLUME 106, JULY 2018, PAGES 67-73

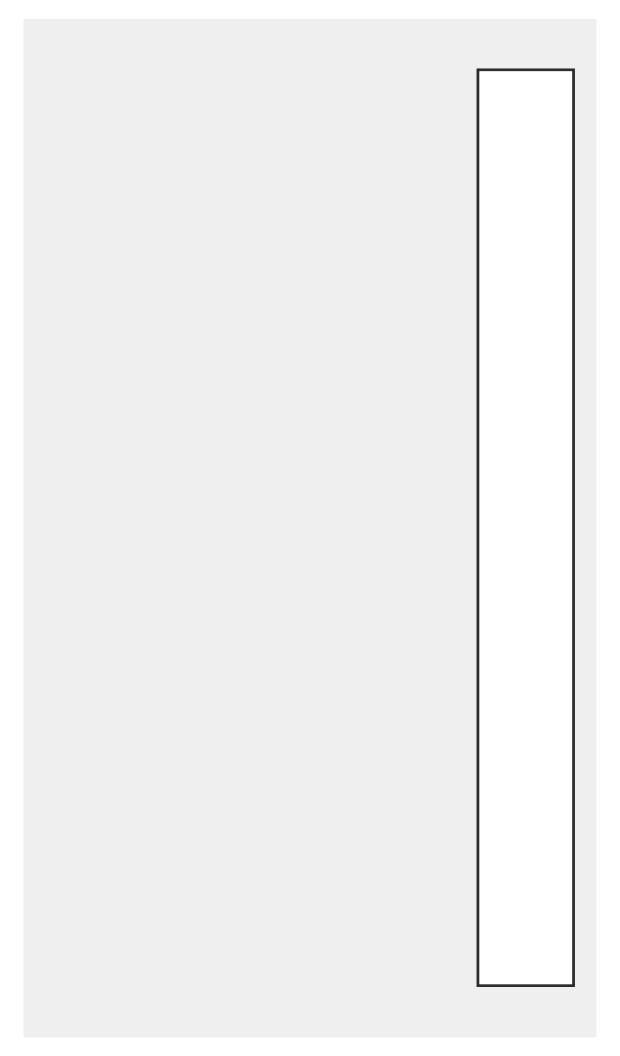
ROGERIO NOGUEIRASOARES^AUGUSTOSCHNE IDERBSANDRA COSTAVALLEBPAULO CAVALHEIROSCHENKEL<sup>C</sup>

#### conclusion

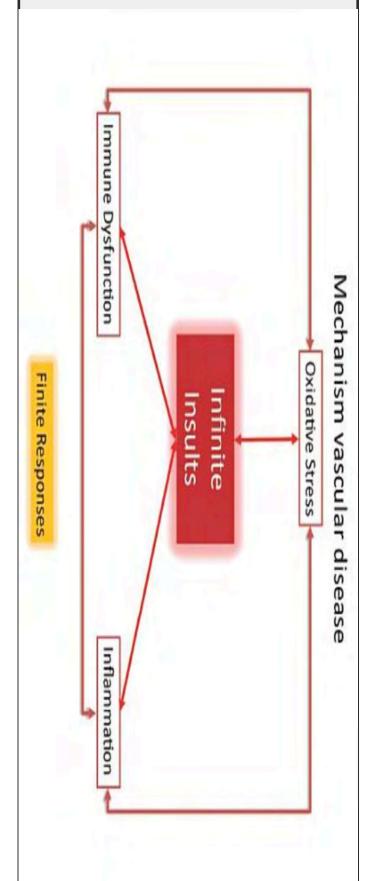
suggest that the influence of the CYP1A2 diastolic blood pressure elevation in cardiovascular hemodynamic changes considered in future studies examining the habitual caffeine consumption should be consumption level. Therefore, genetic physical activity status and caffeine to acute caffeine ingestion is affected by genotypes in basal and post-BP response the AA variant. Additionally, our results response to caffeine ingestion compared to CYP1A2 gene is associated with higher that the presence of the allele C on the The results of the present study indicate induce by caffeine ingestion. actors, physical activity status, and

## SUMMARY OF GENETIC MARKERS

CYP4A11	Apo A2	Apo A1	ADR-B2	NOS3	GSHPx	CYP11B2	Corin		CYP1A2	MTHFR		ApoE	1q25	ACE i/d	COMT				<u>;</u> ! (	4025			6p24.1		9p21 (GG/CC)	Gene Locus
rs1126742	rs5082	rs670	rs1042714	rs1799983	rs1050450 rs3918226 rs1549758	rs1799998	T5551 and Q568P	rs762551	rs2472297	rs1801133 rs1801131	rs7412	rs429358	rs10911021	rs4646994	rs4680		rs10033464	rs10033464	rs2200733	rs2200733	rs499818	rs499818	rs169713	rs2383207	rs10757278	SNP
CTTT	ССС	AA	GG		CC	∄		AA CC AC	⊐	risk table available		risk table available	С	Del	AA GG		ゴ	GT	⊐ ։	7	AA	AG	CC	CC	GG	Genotype Call
Higher hypertension risk	Obesity	Low HDL, CHD, MI	Hypertension and CHD	Ischemic heart disease	CHD, MI and hypertension	Hypertension with high urine and serum aldosterone levels. Poor response to medications with resistance	CHF with low Corin. Low ANP and BNP Increased salt sensitive hypertension.		Increased CHD, MI, hypertension, and arterial stiffness in slow metabolizers	Increased risk for MI and CHD		E4/E4 with increased CHD and MI	Increased CHD in DM		Higher dopamine levels  Low Dopamine levels	Higher Catecholamines Hypertension CHD and MI	1.4x AF and cardioembolic stroke	1.28x AF and cardioembolic stroke	1.5x increased risk for AF and IS	1 4x Atrial Fibrillation and ischemic stroke			CHD and DVT		Heterozygote has 50 % increase risk for MI. Homozygote is 100% increase risk for MI. Also increase risk for DM, AAA	<u>Risk Association</u>
Amiloride		Niacin, Omega 3 FA, some statins.	DASH diet with ACEI or ARB	Nitric oxide precursors	Selenium, glutathione	Low sodium diet and SARA's	Avoid NaCL, increase nitric oxide with diet and arginine.		Avoid caffeine	Methylation treatment		CHD risk factor control	Control glucose. Consider Glutathione or precursors.	TLC to reduce HTN and cardiometabolic risk	Cae of Alfallill Falld Vox pased of COMI	Use of Vitamin E and ASA based on COMT							Early identification, prevention and CHD risk factor control		Aggressive early detection prevention and CHD risk factor contro	<u>Treatment Options</u>



## WHAT TIES ALL THESE GENES TOGETHER?



# SO DO NOT THINK OF THE GENE WORKING THROUGH HYPERTENSION OR HEART DISEASE