Linking of Omics-based Biomarkers with Nutrition and Metabolic Outcomes in Chinese

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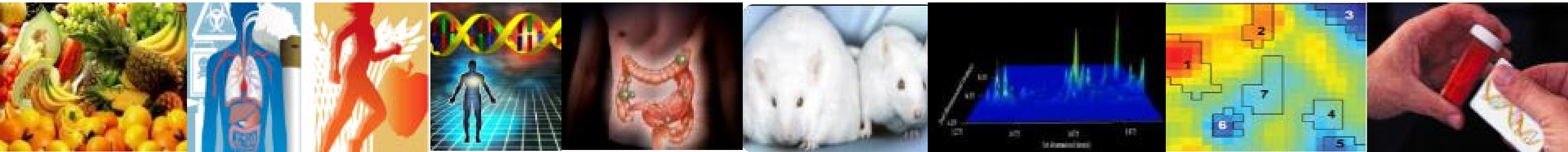


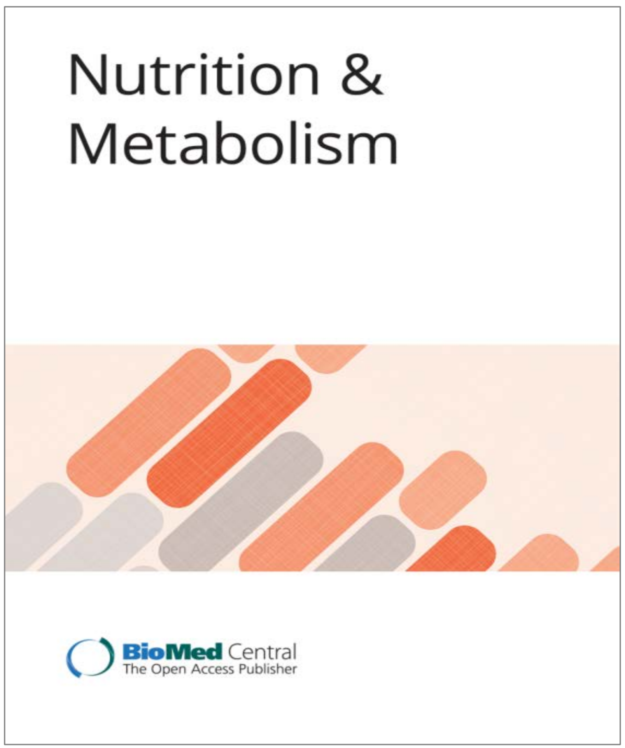
Nutrition & Metabolism Owned by Springer Nature

Editor-in-Chief:

- Dr. Xu Lin
- Dr. Malcolm Watford

Impact Factor:

- 5-yr Impact Fact: 3.525



- Timely and rigorous peer reviewed
  Reputable OA journal over a decade
- The main focused on
  Integrating nutrition, exercise physiology, clinical investigations, and molecular and cellular biochemistry of metabolism.
- Journal scope:
  welcomes studies on molecular, cellular and human metabolism

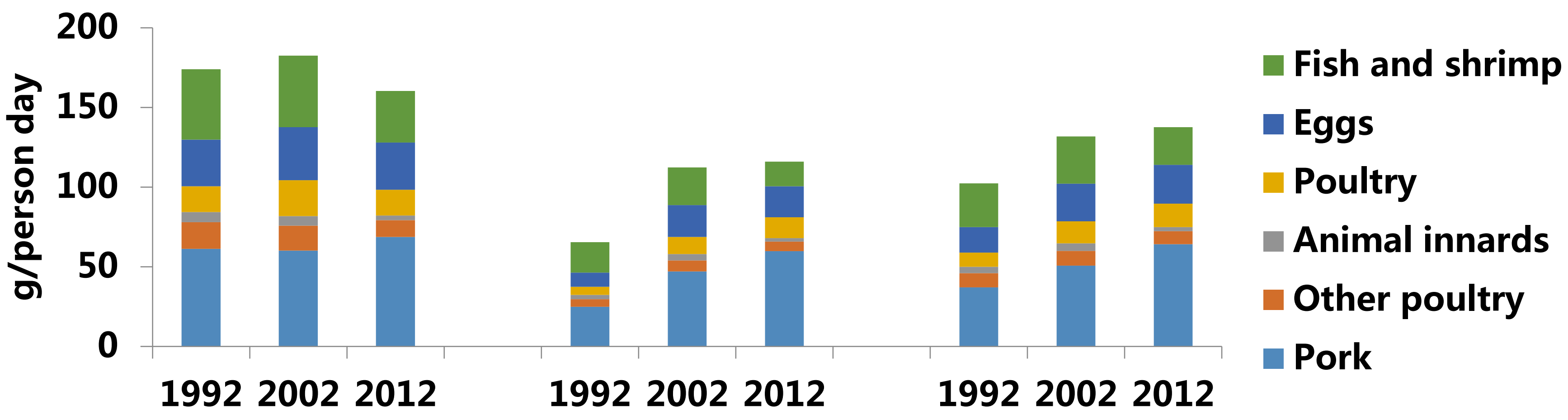
nutritionandmetabolism.biomedcentral.com

Outline

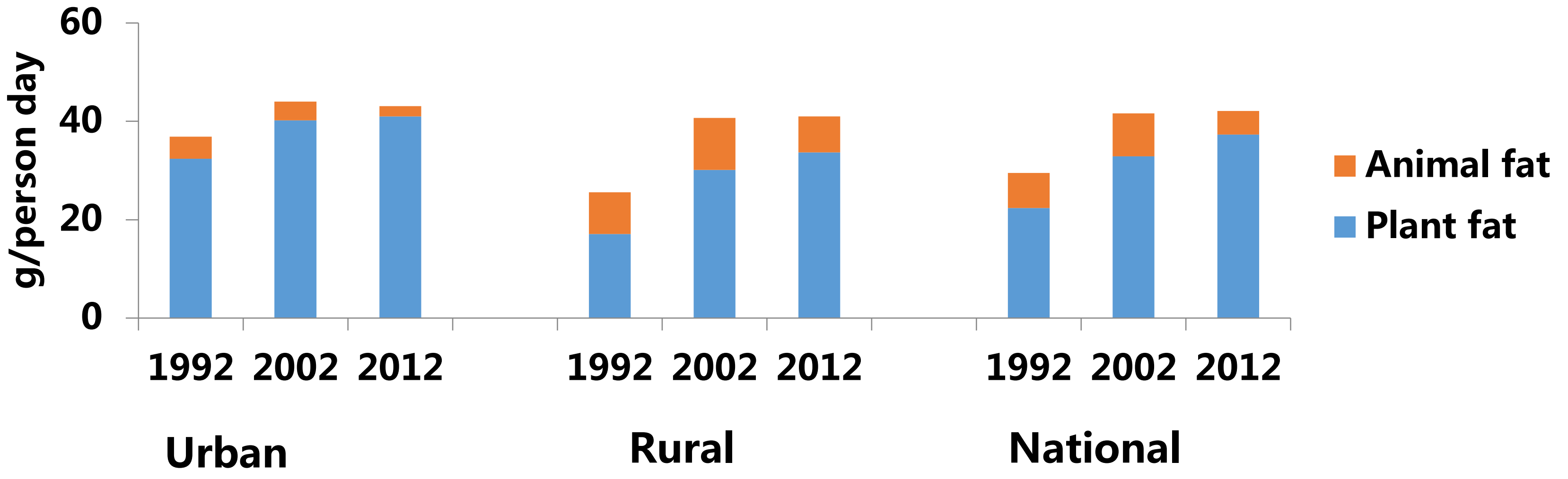
- Background
- Finding from our studies
  - Observational studies
  - Intervention trials
- Currently ongoing studies

Nutrition Transition in China

- ↑ Energy intake from animal foods



- ↑ Energy intake from fats

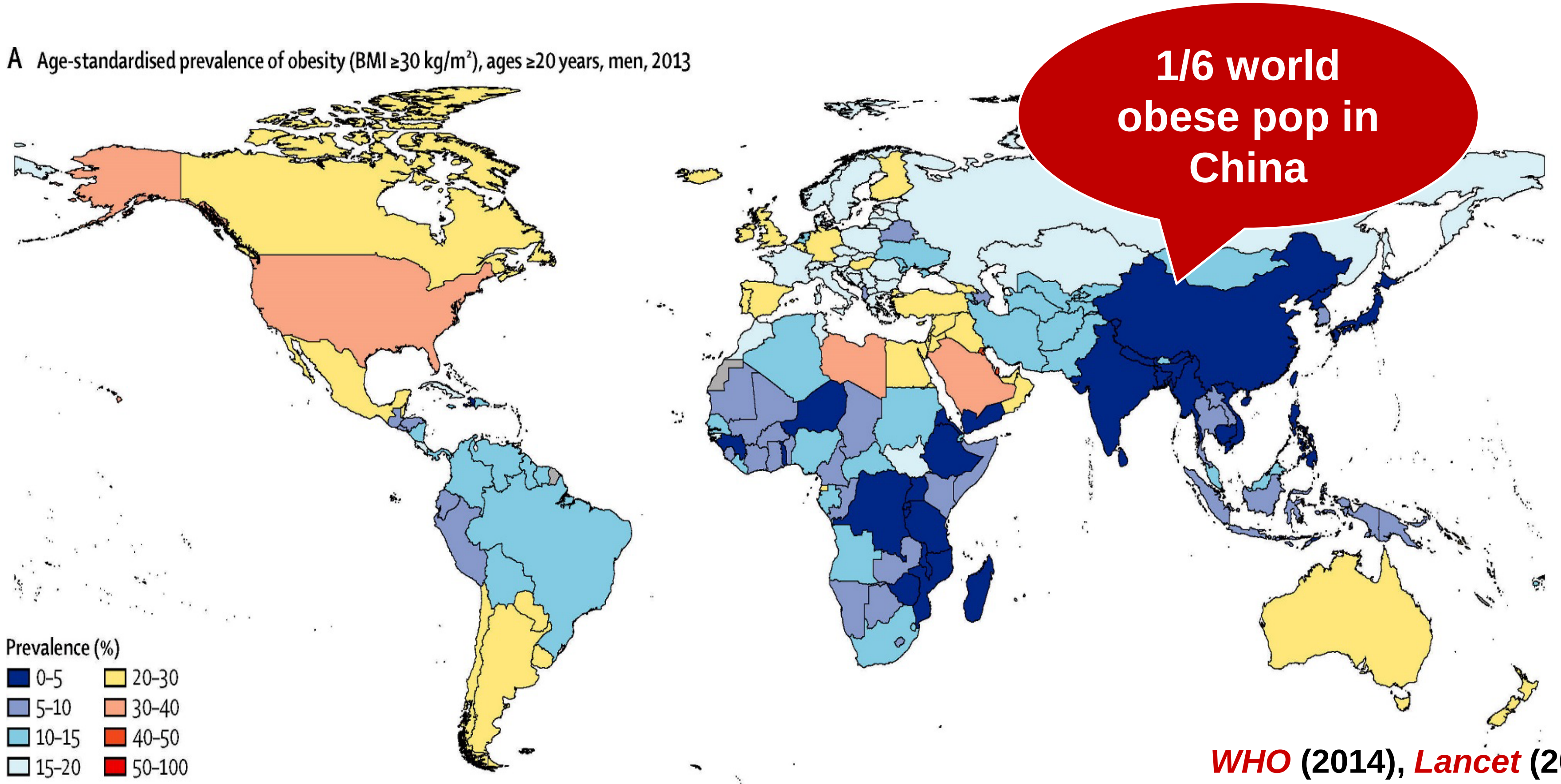


China National Nutrition Survey (2015)

Epidemiology of Obesity

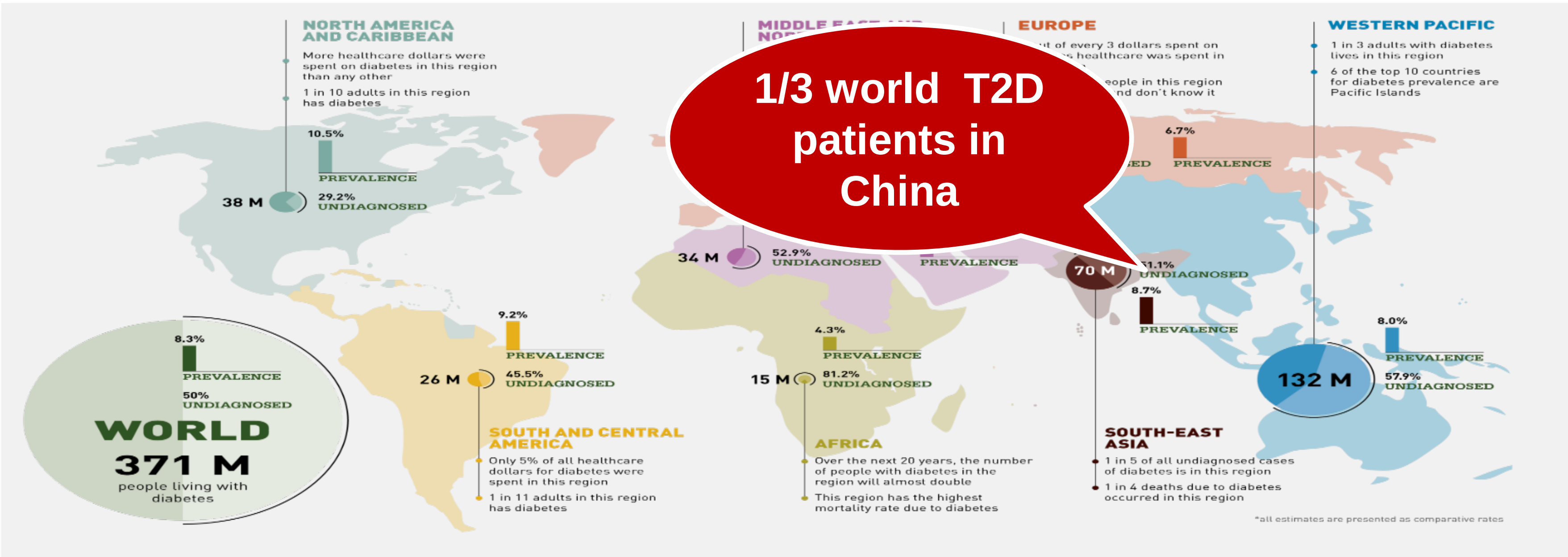
- **Global: 39% adults with overweight , 12.9% adults with obesity**
- **China: 34.4% adults with overweight , 6.9% adults with obesity**

--- the largest obese population in the world

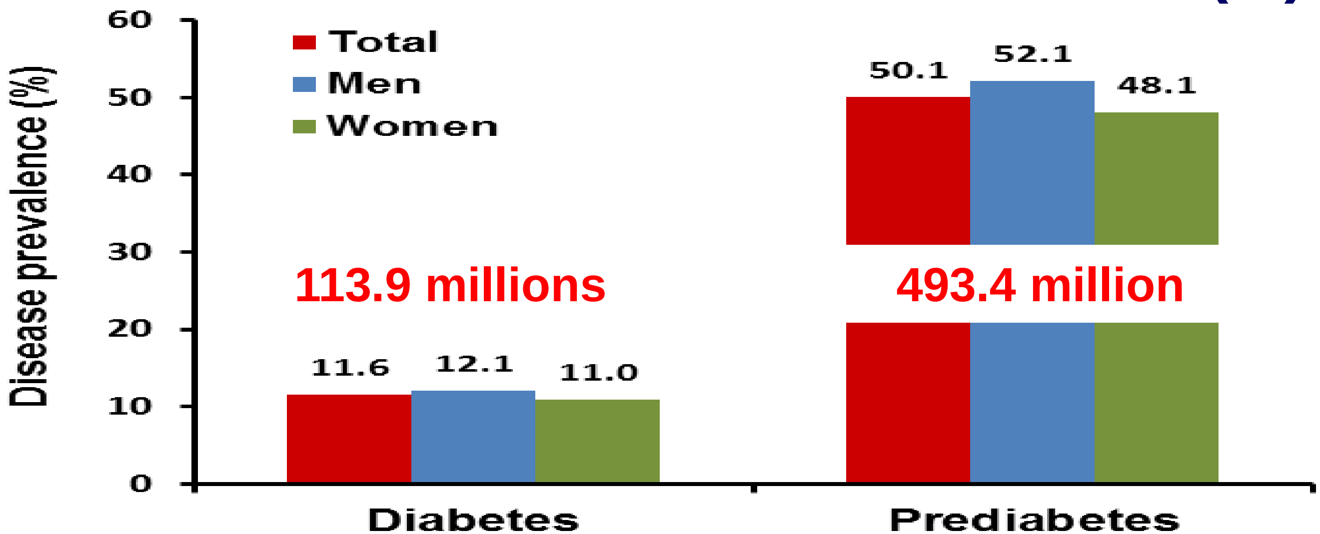


WHO (2014), *Lancet* (2016)

Prevalence of Type 2 Diabetes in Chinese



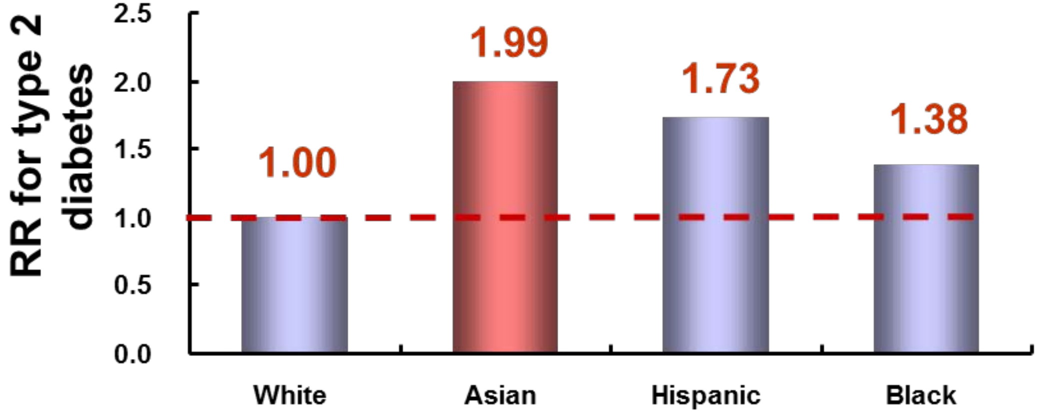
Prevalence of Diabetes in 2012 (%)



JAMA (2013)

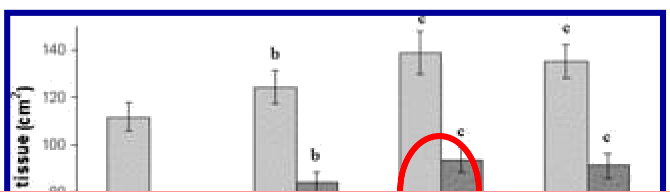
High Susceptibility of Metabolic Diseases in Asians

Multivariate RR of Diabetes among Women with Different Ethnical Backgrounds in the Nurses' Health Study

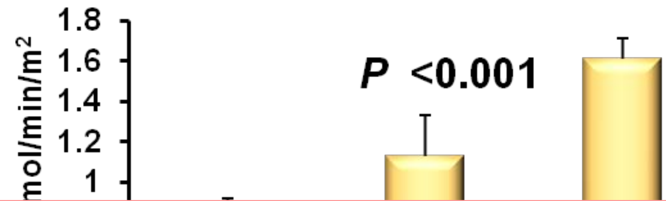


Diabetes Care (2006)

"Metabolic Obesity" in Asians



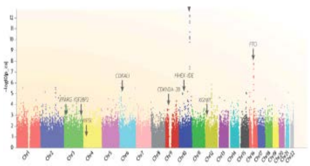
Insulin Sensitivity



Few Chinese cohort studies have systematically investigated the roles of genetic and environmental factors for metabolic diseases

What are nutritional needs and effects of genetic and environmental factors on metabolic risks in Chinese?

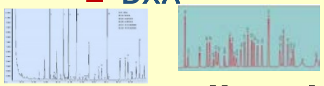
Am J Clin Nutr (2012a)
Hum Genet (2012)
J Lipid Res (2013)



Genetic Factors

Environmental Factors

DXA



Intermediated phenotypes

Nutrition Intervention

Nature (2017)
Nature Med (2017)
Nat Genet (2015，2017)
Diabetes (2008a&b, 2013)
Hum Mol Genet(2009,2016)
Diabetologia (2009, 2010, 2012a, 2014a)
J Lipid Res (2009,2016&17)
J Hyper (2011)

JACC (2007)
JCEM (2007, 2010)
Circulation (2009)
Diabetes care (2010, 2016)
Diabetologia (2014b)
J Nutr (2014)
Endocrine (2016)

JCEM (2008, 2012)
J Nutr (2008, 2013ab)
Diabetes Care (2009, 2014)
Diabetologia (2012b)
Am J Clin Nutr (2012b, 2013)
Int J Epidemiol (2015)
J Epidemiol Commun H (2016)

PLoS One (2007)
Am J Clin Nutr (2009)
Br J Nutr (2009,2013)
J Nutr (2009,2010,2011)
Eur J Nutr (2013, 2016ab)
JCEM (2017

Nutritional Needs
Obesity, Metabolic Syndrome (MetS)
Type 2 Diabetes (T2DM)

Outline

- Background
- Finding from our studies
  - Observational studies
  - Intervention trials
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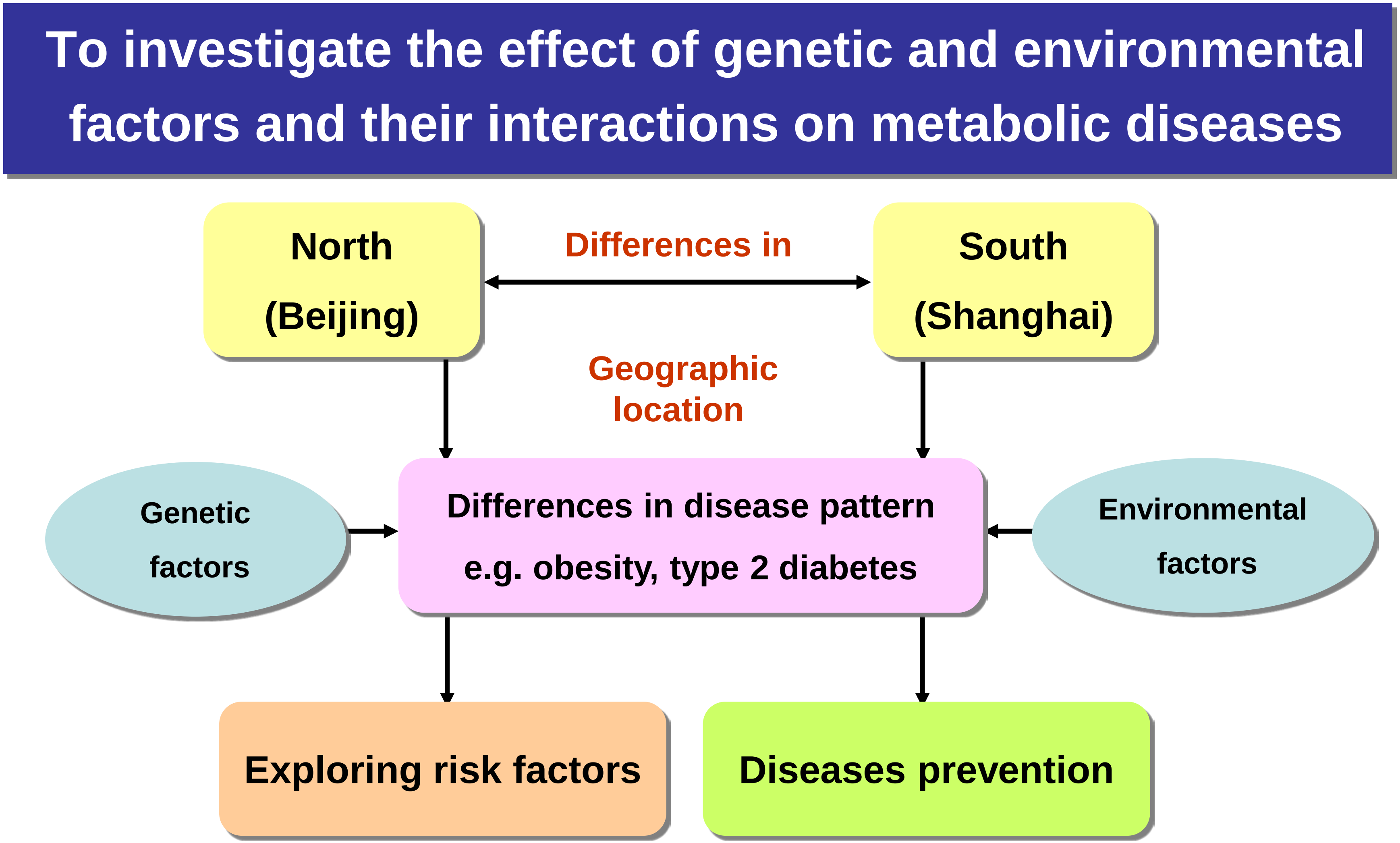
Nutrition and Health of Ageing Population in China



Nutrition and Health of Ageing Population in China

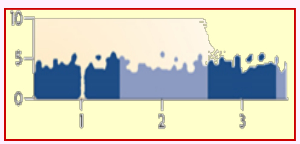
Baseline	Gene & Environment	Phenotype	Disease

Beijing
(n=1600)

Shanghai
(n=1600)

Genetic factors

- GWAS database
  - 2M SNPs
  - 100k CNVs
- Exome SNPs



Environments

- Diet
- Lifestyle
- Mental health

Anthropometric Data:

BP, BMI, waist/hip
body composition (DXA)

Biomarkers:

- CRP, IL6, TNFR1/2
- Adiponectin, RBP4, Resistin, PAI-1
- Glucose, Insulin, lipids, HbA1c
- Ferritin, vitamin D, vitamin B1
- Fatty acids profile
- Amino acids profile
- Acylcarnitine profile
- Ionomic profile

- Type 2 diabetes
- Metabolic syndrome
- Cardiovascular disease
- Kidney function decline
- ….

2005 2011

GWAS Database for Obesity and Type 2 Diabetes

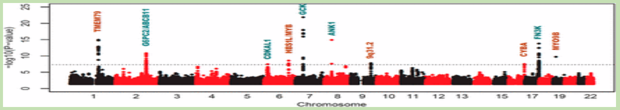
Lead National Type 2 Diabetes GWAS in China

- **Identified 2 novel (*RASGRP1* and *GRK5*), 23 reported loci for T2D in ~43,000 individuals**
- **Acquired >0.56M SNPs covering >92% common variants and >1000 common CNVs in Chinese**
- **Acquired >15M SNPs and CNVs imputed from HapMap and 1000Genome**

Lead and joining >10 international GWAS collaborations

- **Obesity: 15 novel loci, 62 reported loci**
- **Height: 17 novel loci, 81 reported loci**
- **Blood pressure: 27 novel loci, 23 reported loci**
- **HbA1c: 4 novel loci, 5 reported loci**
- **Fatty acids: 7 novel loci, 11 reported loci**

Hum Mol Genet **(2016)**



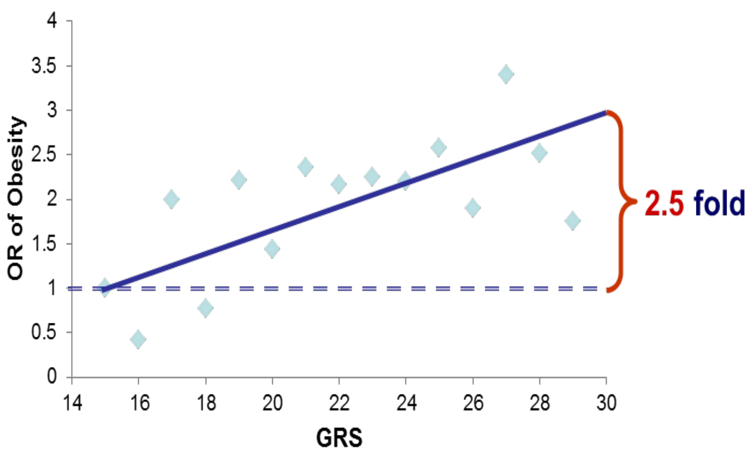
AGEN Asian Genetic Epidemiology Network · DIAGRAM · GIANT CONSORTIUM

Nature **(2017),** ***Nat Genet*** **(2015, 2017),** ***Nature Med*** **(2017),** ***JAMA oncology*** **(2016) ,** ***Hum Mol Genet*** **(2016, 2014&2012),** ***Diabetes*** **(2013),** ***Hypertension*** **(2013),** ***Diabetes*** **(2013),** ***Diabetologia*** **(2014, 2012, 2011&2010)** ***J Lipid Res*** **(2013, 2017),** ***AJCN*****(2012),** ***PLoS Genet*** **(2010)**

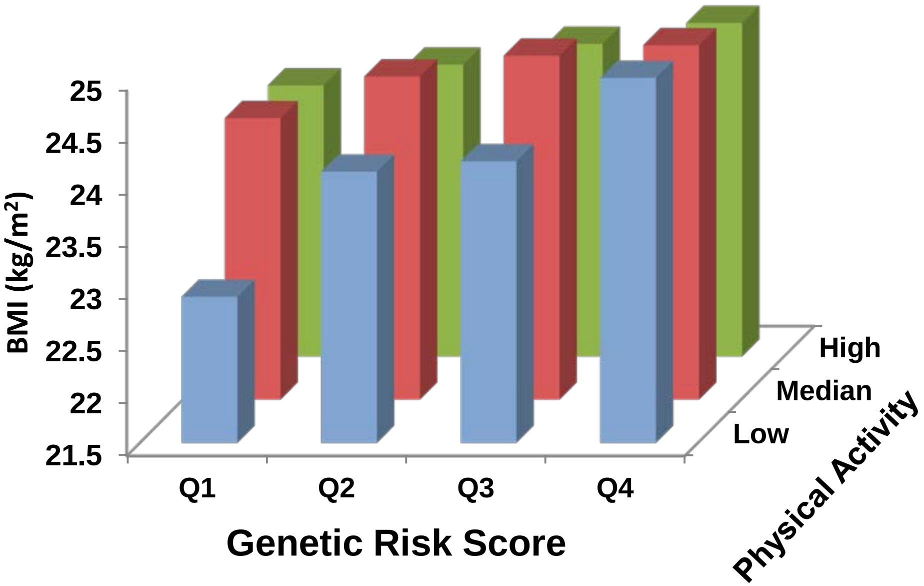
Genetic Predisposition of Obesity

- ↑ Genetic Risk Score (28 BMI-increasing risk loci like *FTO*, *MC4R*, *PCSK1*), ↑BMI, ↑ total and trunk fat percentage (DXA)
- ↑ Physical activity ↓ genetic predisposition for raising BMI

Each additional BMI-increasing risk allele ↑ 7% obesity risk



↑ Physical Activity
↓ Genetic Predisposition of ↑ BMI

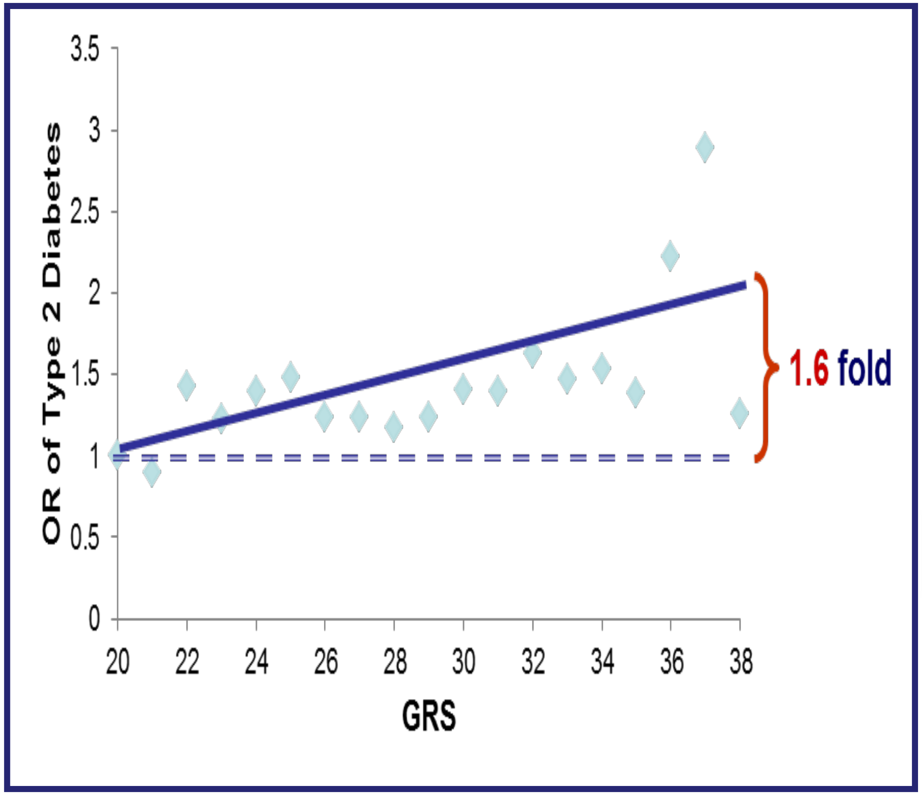


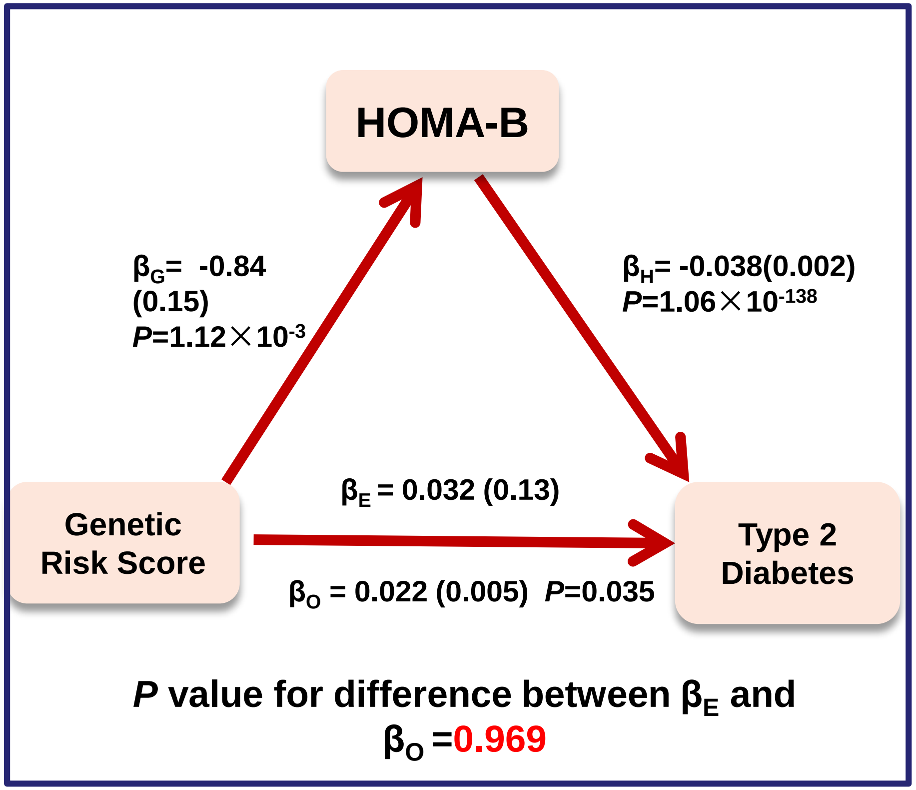
P for interaction=0.022

PLoS One (2014)

Genetic Predisposition of Obesity with Diabetes

- ↑Genetic Risk Score (30 BMI-increasing risk loci, like *FTO*, *MC4R* and *PCSK1*) was associated with ↑ T2D
- The association was independent of BMI in Chinese, partly mediated by HOMA-B



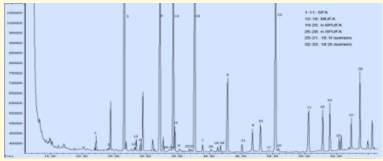


Diabetologia (2014)

Established Erythrocyte Fatty Acid Database

A total of 28 types of fatty acids were detected in 3252 participants

- **Trans FA**
  18:1t isomer 18:2n6 9c12t   18:2n6 9t12c
- **PUFA n-6**
  18:2n6   18:3n6   20:2n6   20:3n6   20:4n6   22:2n6   22:4n6   22:5n6
- **PUFA n-3**
  18:3n3   20:5n3   22:5n3   22:6n3
- **SFA**
  14:0   16:0   18:0   20:0   22:0   24:00
- **MUFA**
  16:1n9   16:1n7   18:1n9 18:1n7 20:1n9   22:1n9   24:1n9

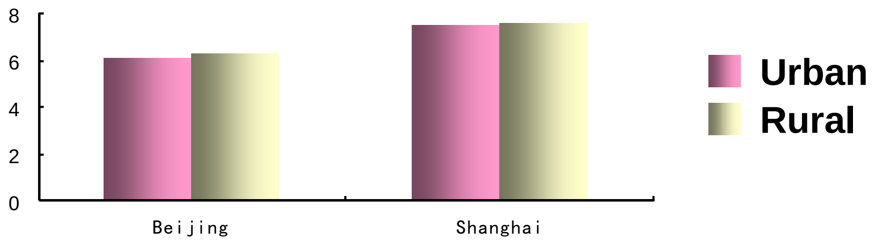


GC-FID

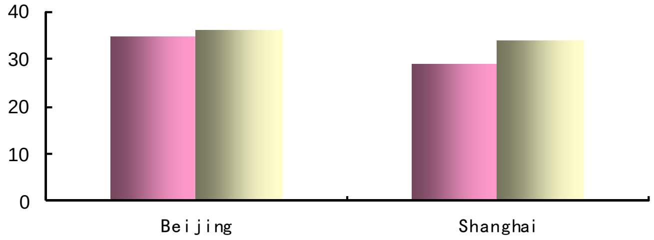
- **Most of cohort studies were from western populations**
- **Commonly used dietary questionnaires could introduce many measurement errors**
- **Erythrocyte fatty acids reflect relatively long-term of intakes** (essential and trans fatty acids)**, particularly important for countries without relevant food composition database like China**
- **Evidence regarding the relationships of blood fatty acids with MetS or T2D is limited, and remains controversial**

n-3 Fatty Acids and Metabolic Syndrome

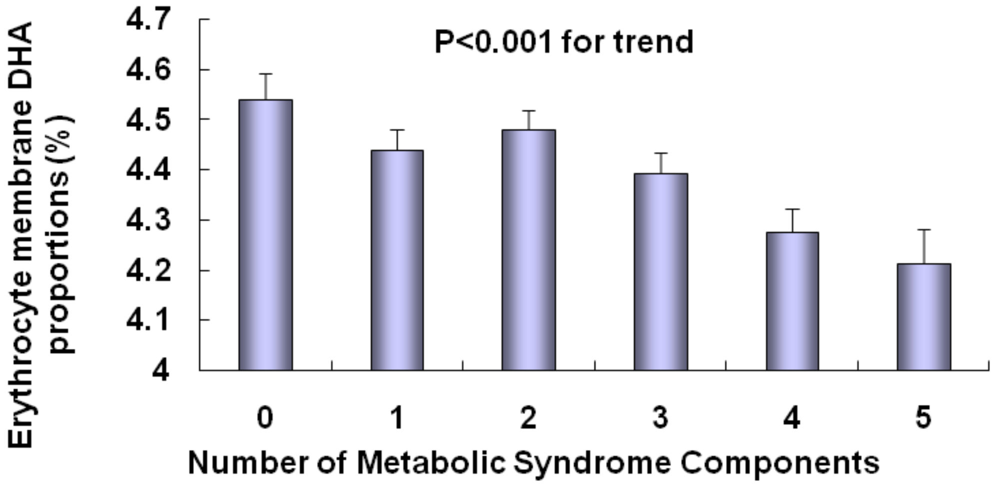
↑Fish Intake are Associated with ↑n-3 FA in Shanghai



↑Plant Oil Intake are Associated with ↑n-6 FA in Beijing



↓DHA ↑Number of Metabolic Syndrome Components

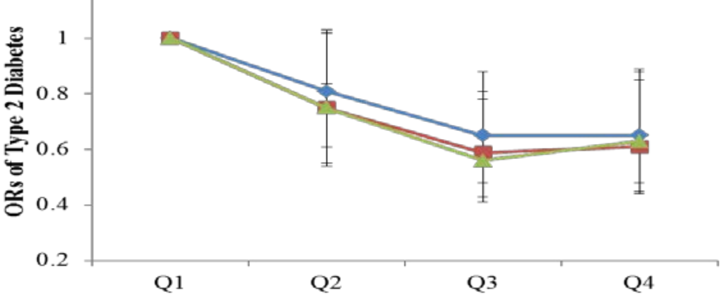


JCEM (2012)

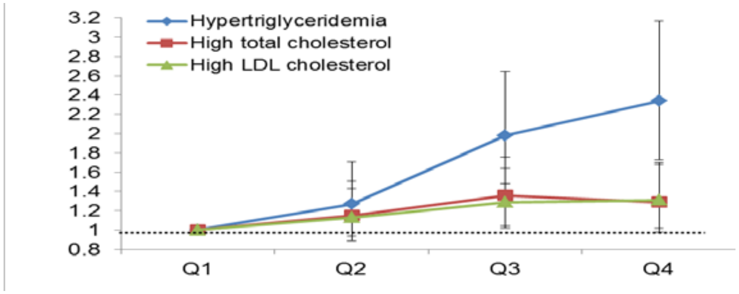
Trans-Fatty Acids and Metabolic Disorders

- **Total of TFAs are low (0.37 % *vs* 1.8 % in US studies)**
- **Trans-18:1 isomers (>50% of total TFA) was associated with dairy products**

↑ Trans-18:1 was associated with ↓ T2D risk

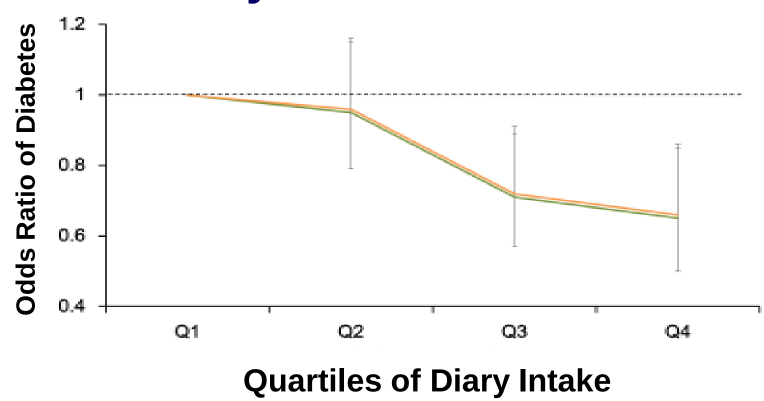


↑ Trans-18:2 was associated with ↑ dyslipidemia risk



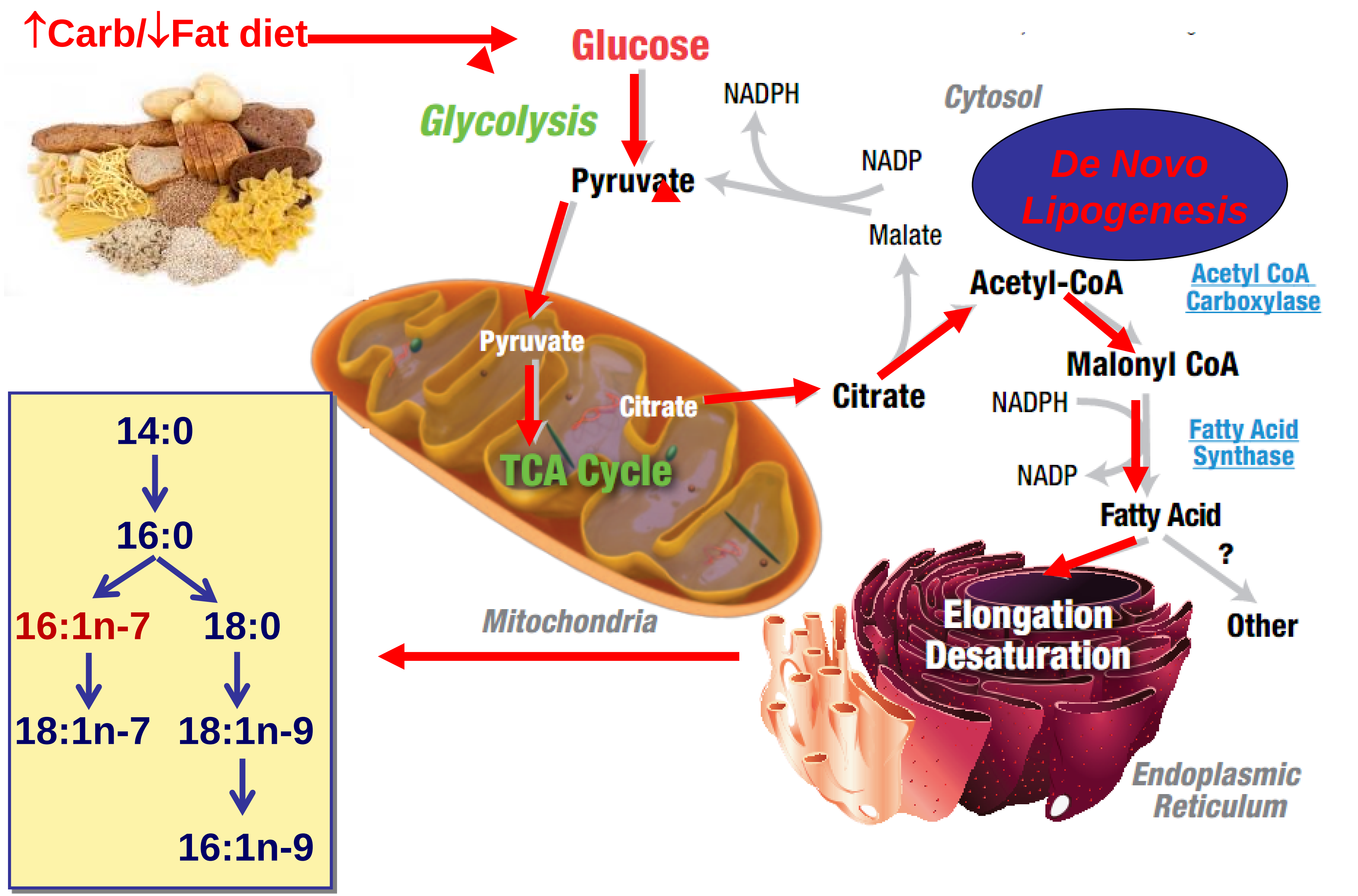
The association between ↑ Trans 18:1 and ↓ 6-yr T2D Incidence was dairy dependent

↑Dairy intake was associated with ↓ 6-yr T2D Incidence



***Diabetologia* (2012) *Diabetes Care* (2014)**

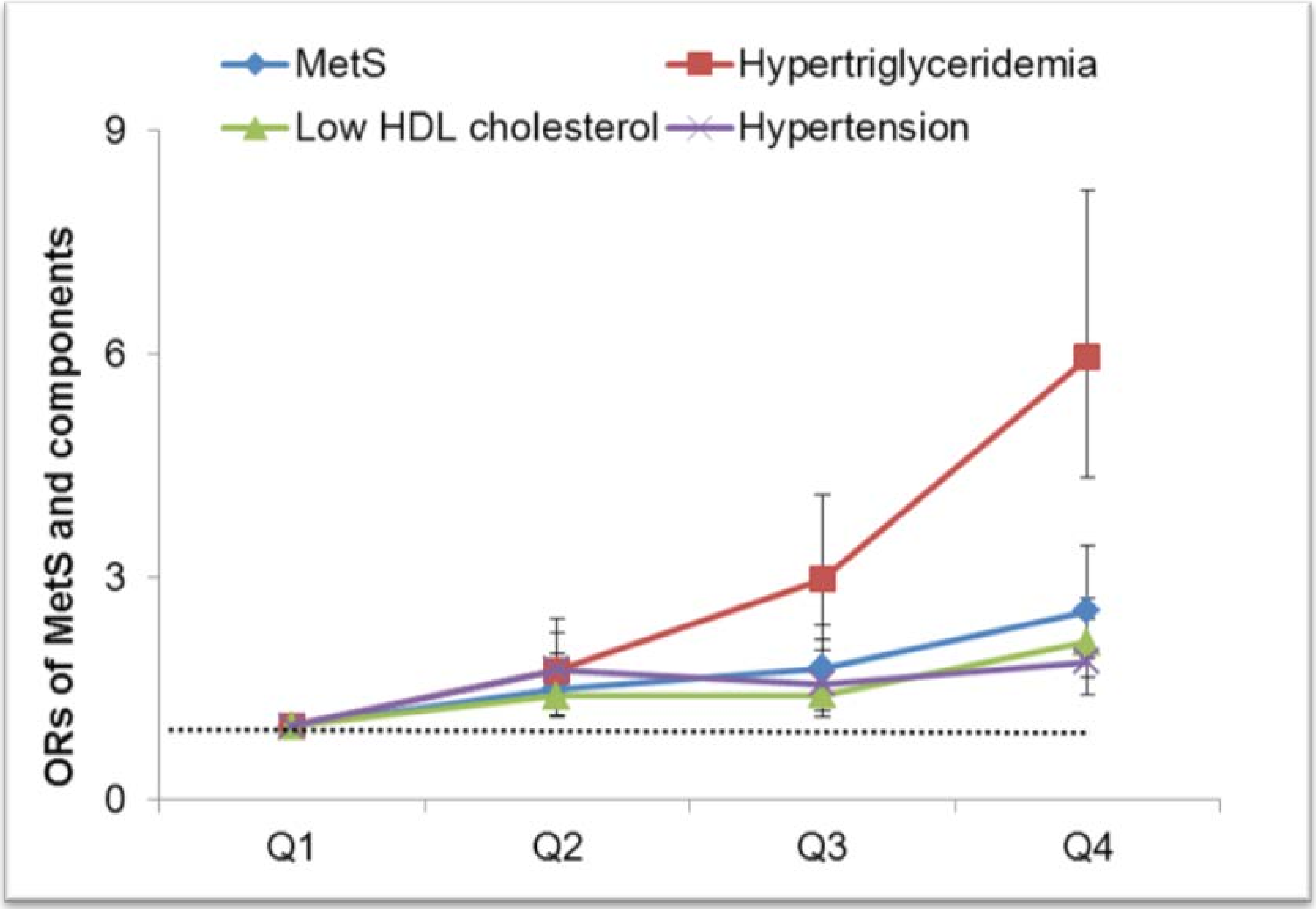
Carb Intake and *De Novo* Lipogenesis (DNL)



Adapted from ASBMB 2012

DNL Fatty Acid and Metabolic Syndrome - Baseline

↑16:1n-7 was Associated with ↑ MetS Risk and Its Components

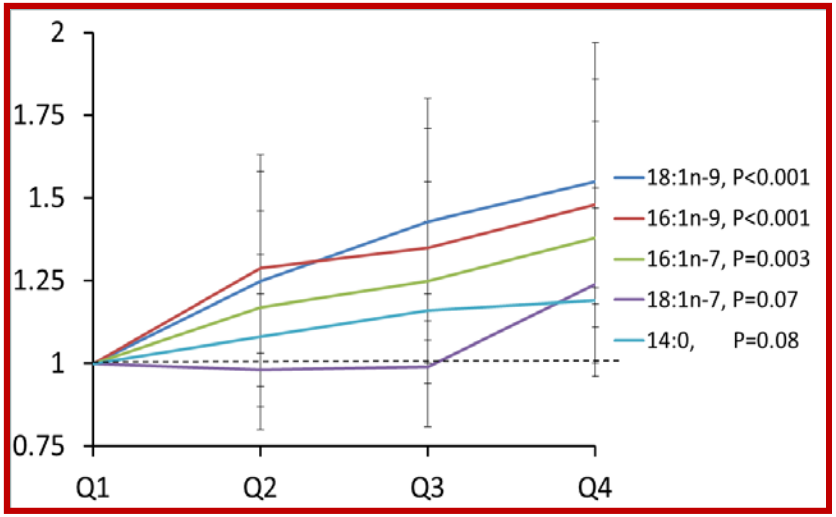


Am J Clin Nutr **(2012)**

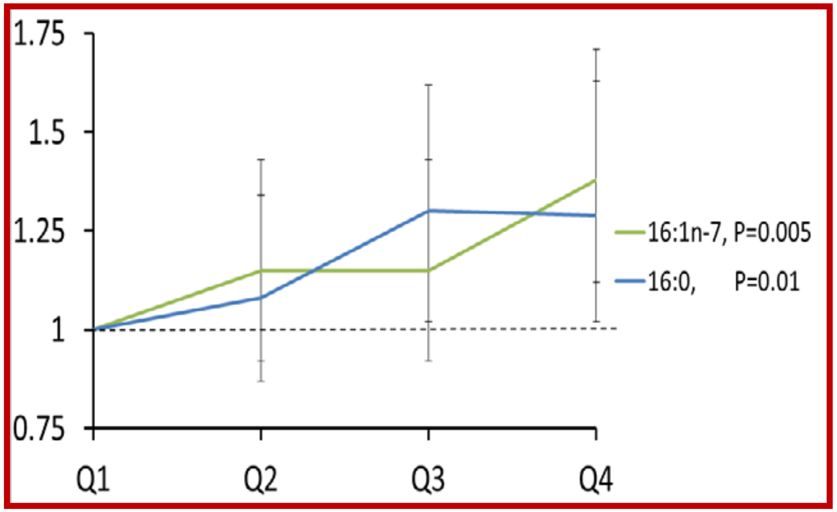
DNL Fatty Acids and 6-yr Risks of Metabolic Disease - Cohort

- ↑ DNL fatty acids were associated with ↑ 6-yr incident MetS by 30-51%
- ↑ DNL fatty acids associated with ↑ 6-yr incident T2DM by 20-30%

↑ 16:1n-7, 16:1n-9, and 18:1n-9
↑ 6-yr Incident MetS



↑ 16:0 and 16:1n-7
↑ 6-yr Incident T2DM



- Model 1: adjusted for age, sex, region, and residence
- Model 2: Modle1+ physical activity, education attainment, current smoking and drinking, family history of chronic diseases, total energy intake, carb intake of total energy, and energy-adjusted dietary glycemic index and energy-adjusted glycemic index;
- Model 3: Modle2+ BMI

Am J Clin Nutr **(2013)**

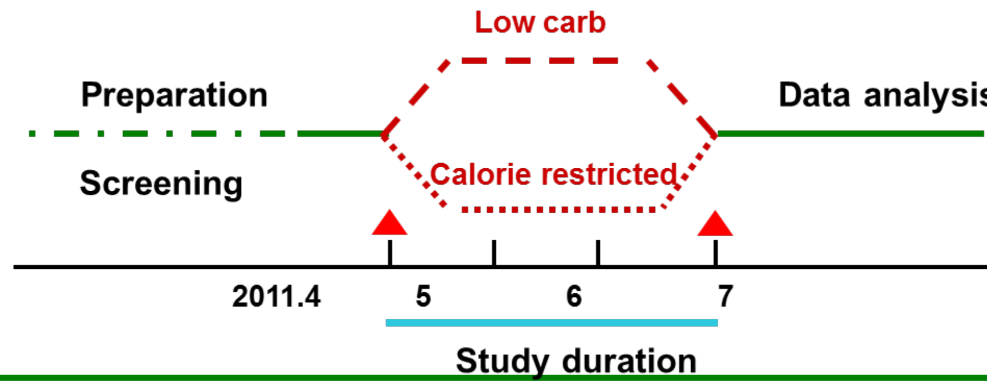
Low Carb Intervention Reduced Erythrocyte 16:1n7

Design: A randomized, controlled and parallel trial

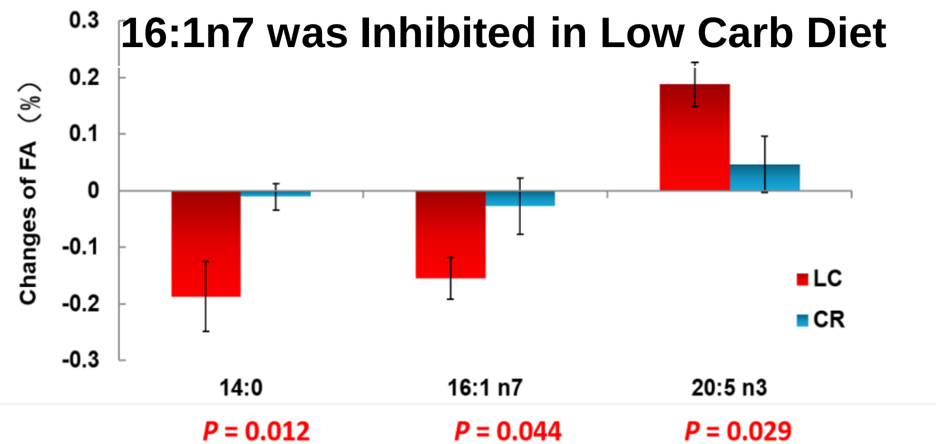
Subjects: 50 volunteers (BMI ≥ 24 kg/m^2)

Duration: 12 weeks

- Low Carb Group
  Carb: 20-120 g/d
- High Carb + ↓Calorie Group
  35% calorie restricted
  Carb: 55%; protein: 19%; fat:26%

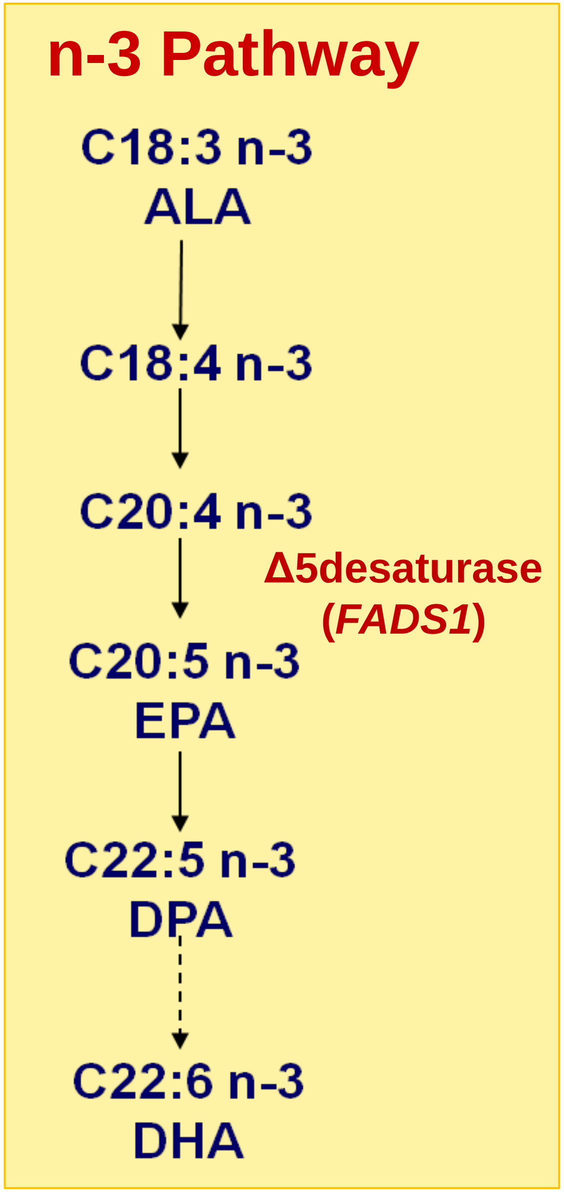


- Both diets ↓ (~5 kg BW)
- Low carb diet ↑ HDL-C
- Low carb diet ↓ 16:1n7

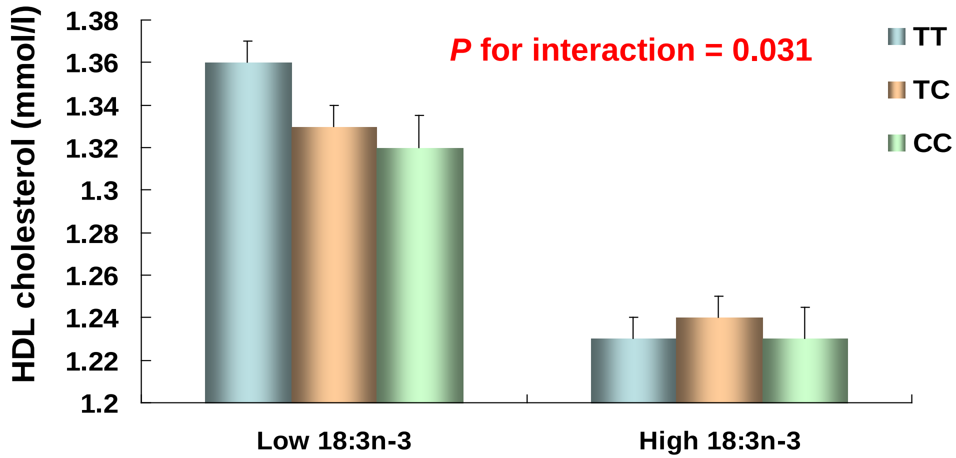


Br J Nutr (2013)
Unpublished data

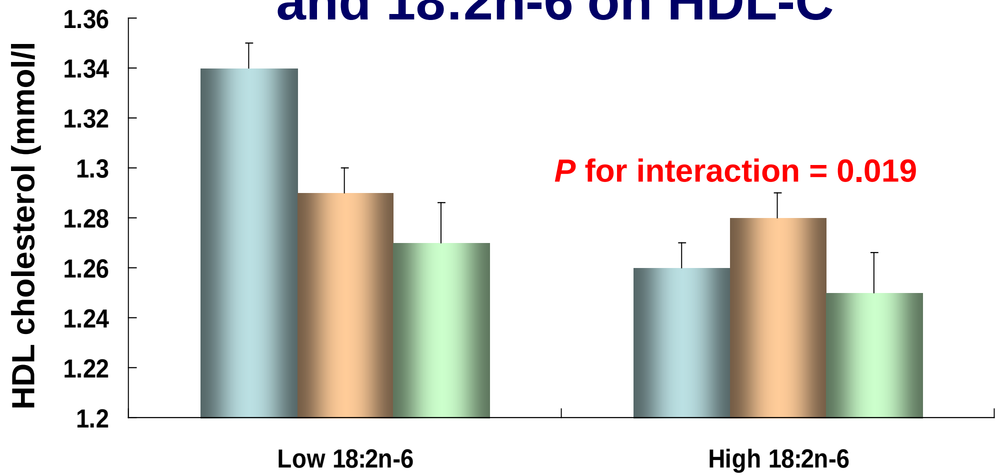
Interaction of Variant in *FADS1* and PUFA on Lipid Profile



Interaction between *FADS1*-rs174550 and 18:3n-3 on HDL-C



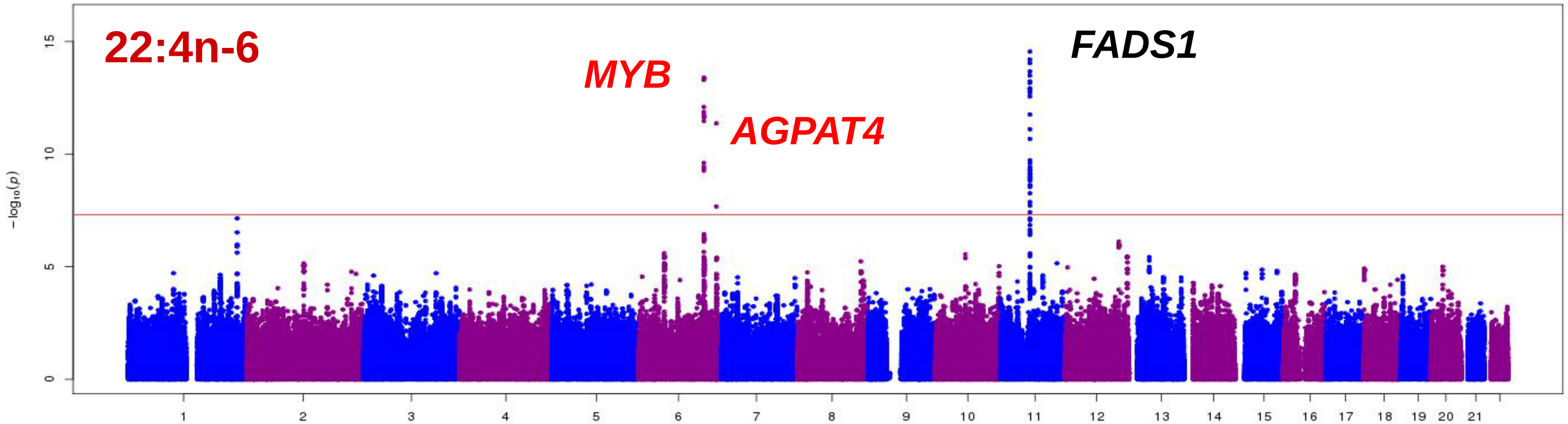
Interaction between *FADS1*-rs174550 and 18:2n-6 on HDL-C



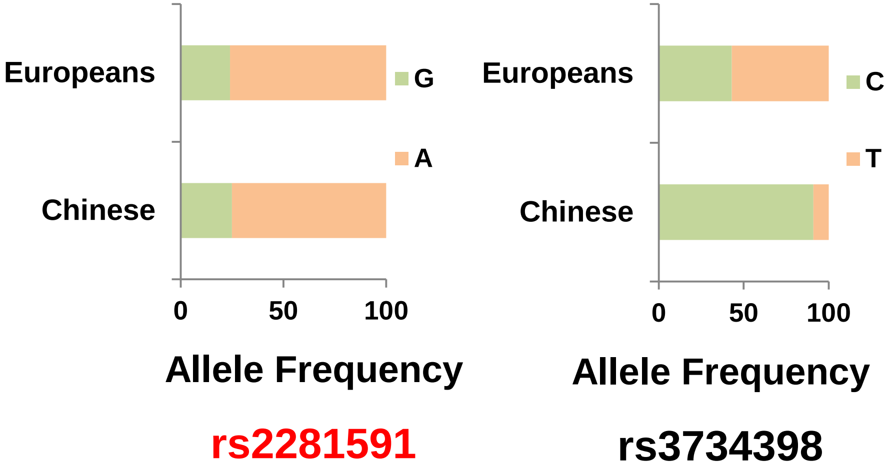
J Lipid Res **(2013)**

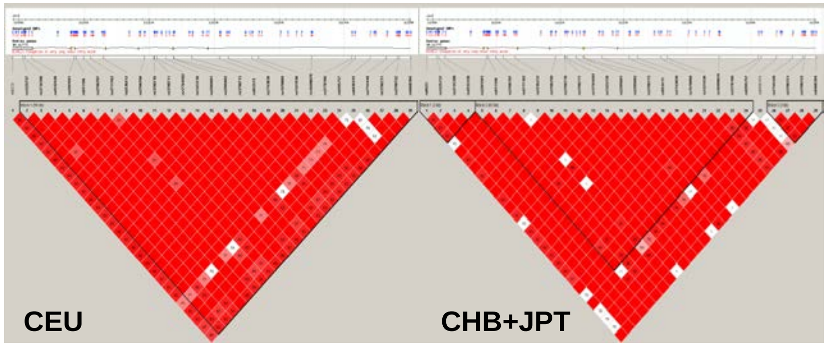
GWAS Meta of PUFA in Chinese and Europeans

Identified 2 Novel Loci (*MYB* and *AGPAT4* for 22:4n-6) in Chinese



Identified 1 Independent Signal (rs2281591) at *ELOVL2* for 22:5n-3 in Chinese



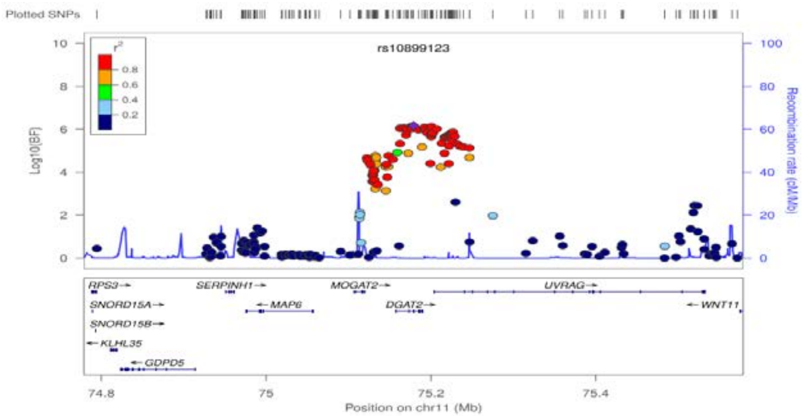


Hum Mol Genet (2016)

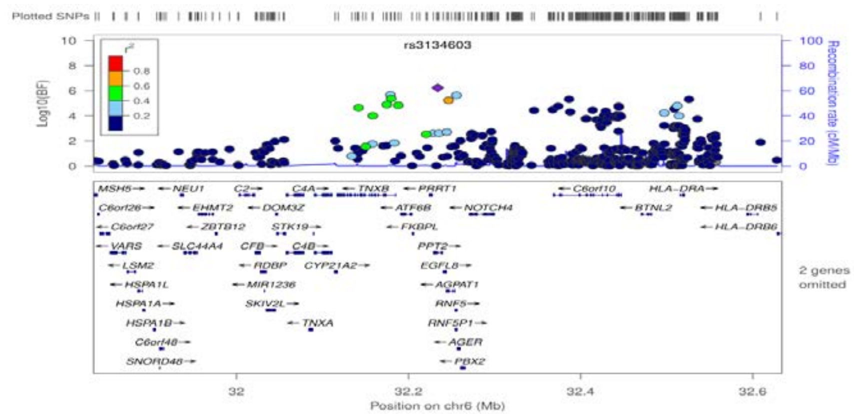
GWAS Meta of PUFA in Chinese and Europeans

Trans-Ethnic Meta
Identified 2 Additional Novel and Confirmed 5 Loci

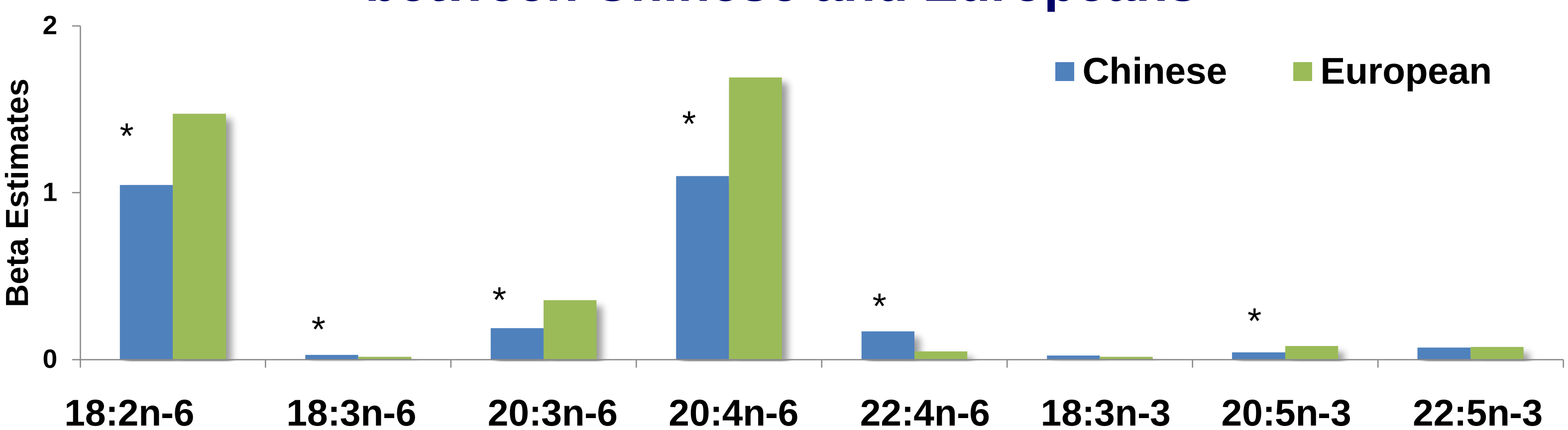
DGAT2-rs10899123 for 18:3n-6



PPT2-rs3134603 for 22:5n-3



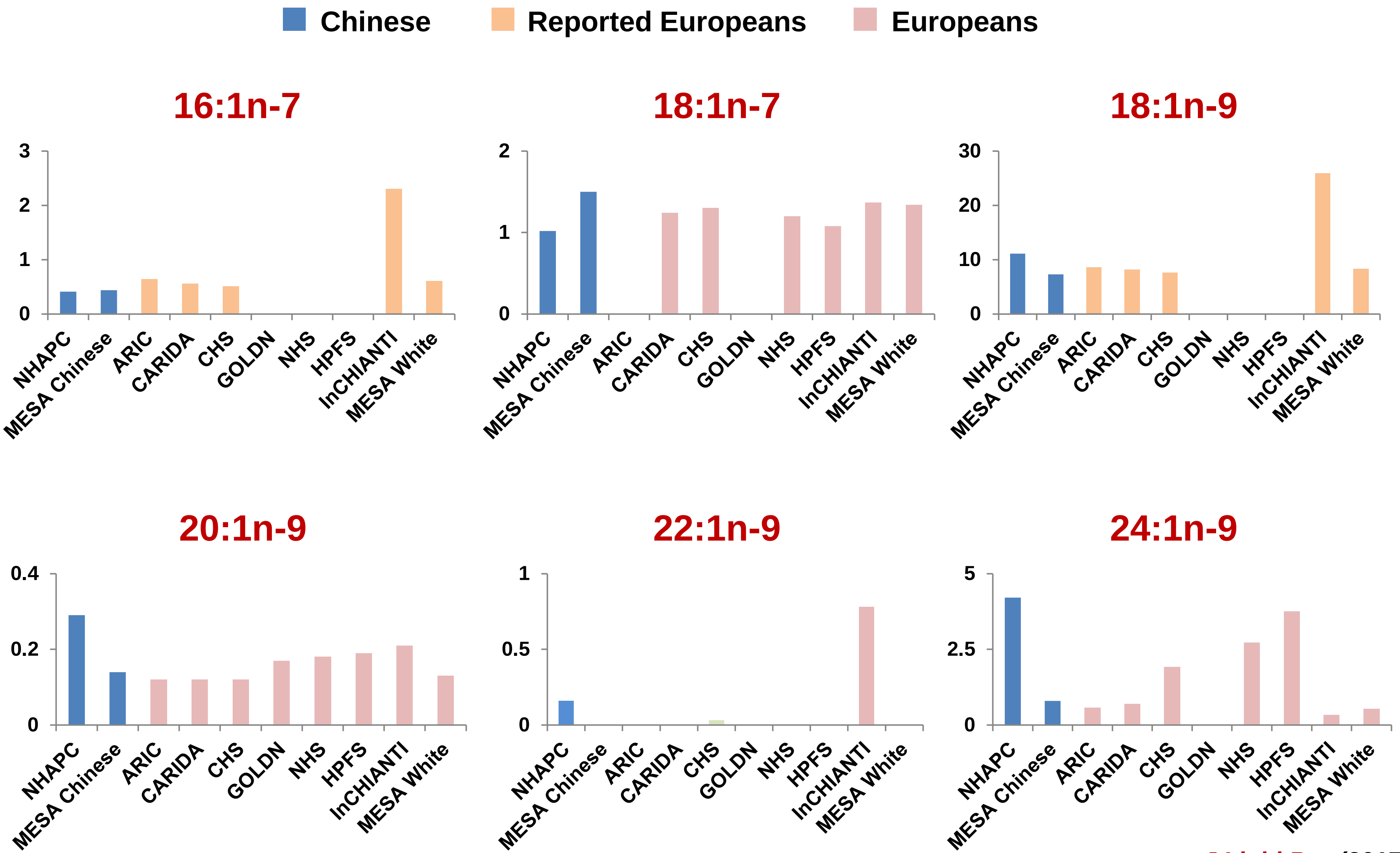
Different Effect Sizes of *FADS1* Variants on PUFA Levels between Chinese and Europeans



Hum Mol Genet (2016)

GWAS Meta of MUFA in Chinese and Europeans

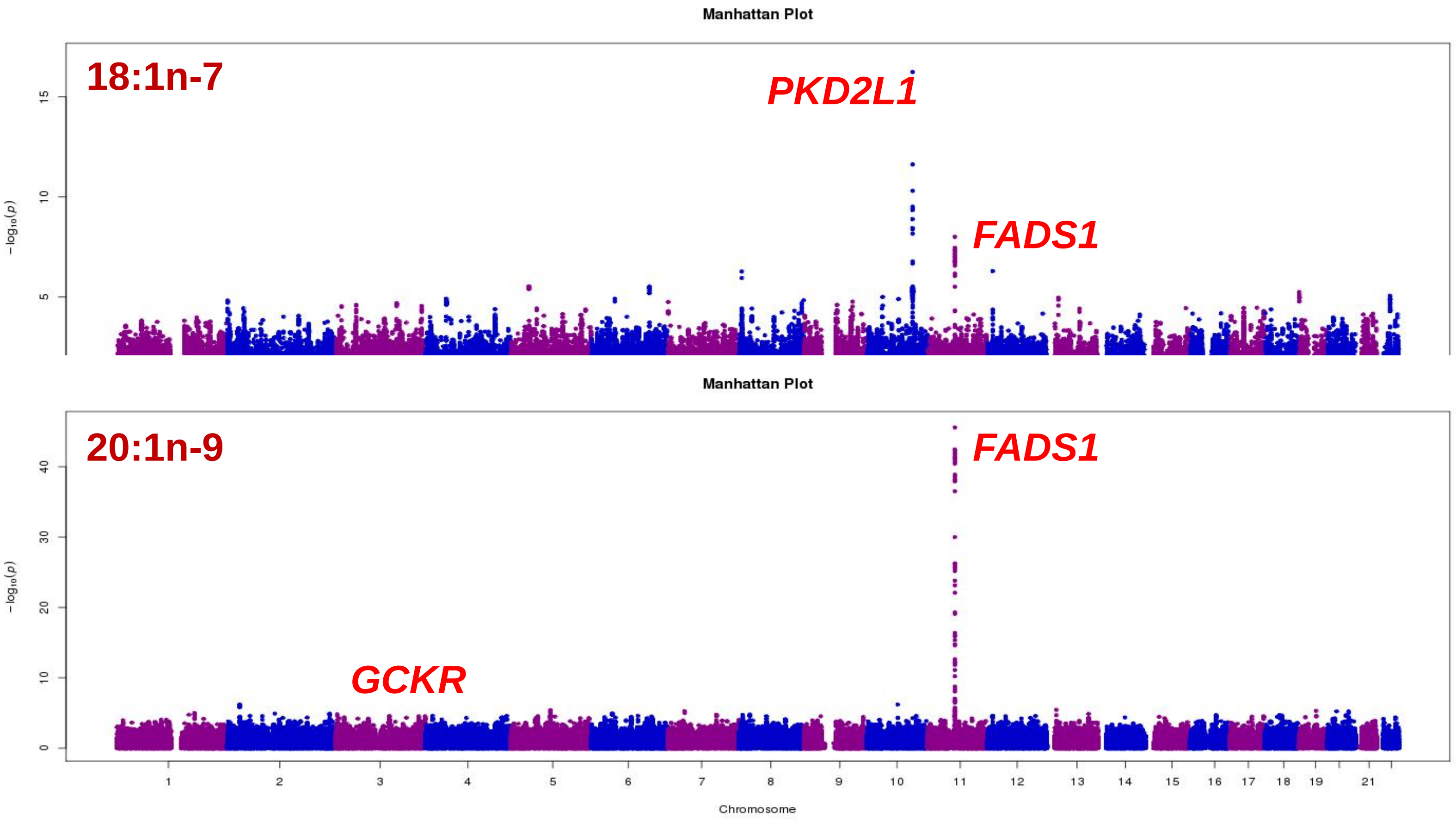
MUFA Profiles in Chinese and Europeans



J Lipid Res (2017)

GWAS Meta of MUFA in Chinese and Europeans

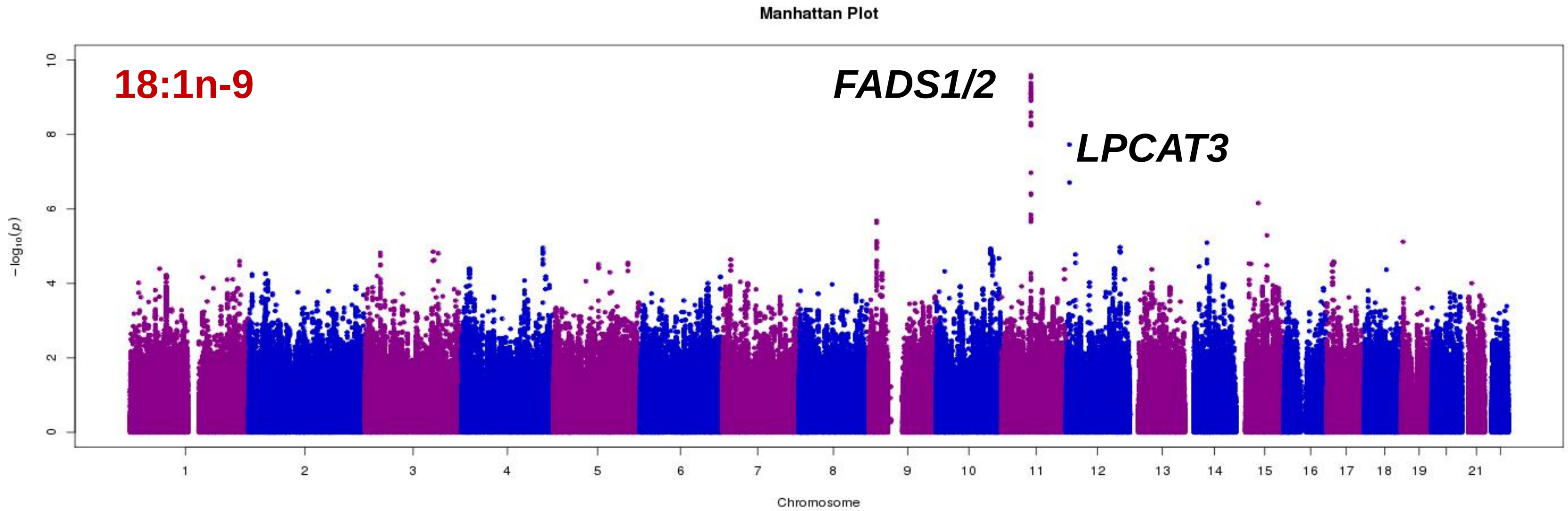
Trans-Ethnic Meta found 4 Novel Associations

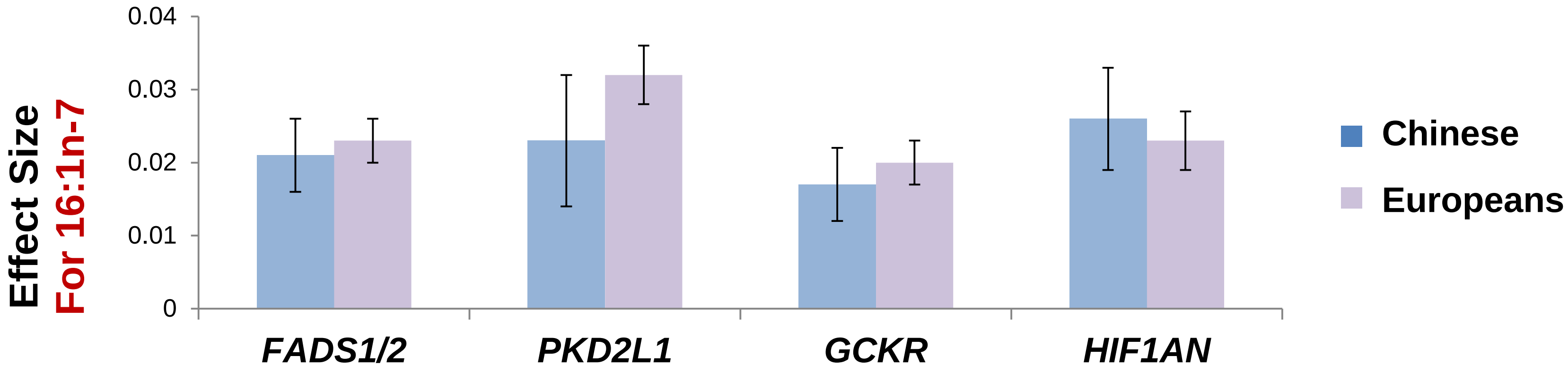


J Lipid Res **(2017)**

GWAS Meta of MUFA in Chinese and Europeans

Trans-Ethnic Meta Confirmed 6 Reported Associations

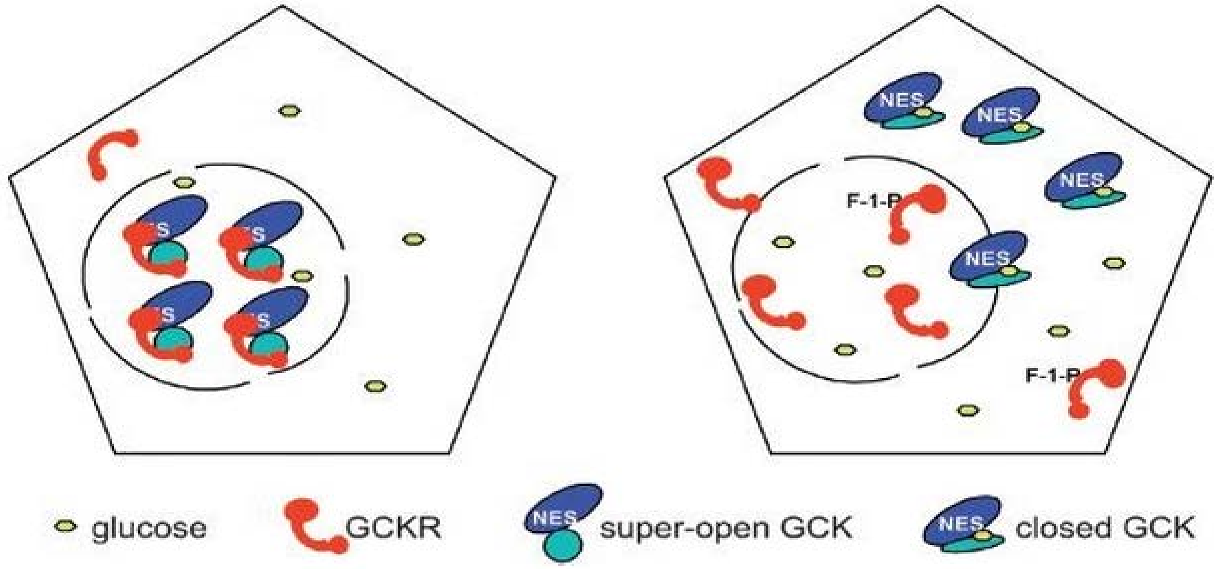




J Lipid Res (2017)

Potential Functional SNP at *GCKR*

GCKR: Encodes glucokinase (GCK) regulator (GCRP)



Hum Mol Genet 2009

Glucose —GCK→ Acetyl-CoA ➡ 16:0 ➡ 16:1n-7

Functional Studies: rs1260326-T ➡ GKRP-Leu ➡ ↑ GCK activity

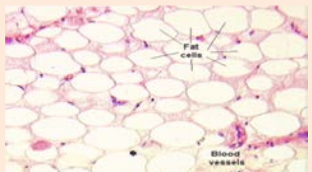
Our GWAS: rs1260326-T ➡ ↑16:1n-7

J Lipid Res (2017)

Potential mechanism of SNP at *PKD2L1*

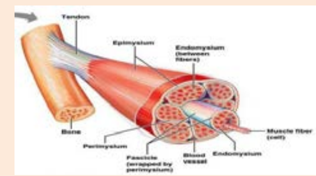
PKD2L1-rs603424 might influence 16:1n-7 and 18:1n-7 levels by ↓ expression of *SCD* (Δ9 desaturase)

Adipose Tissue



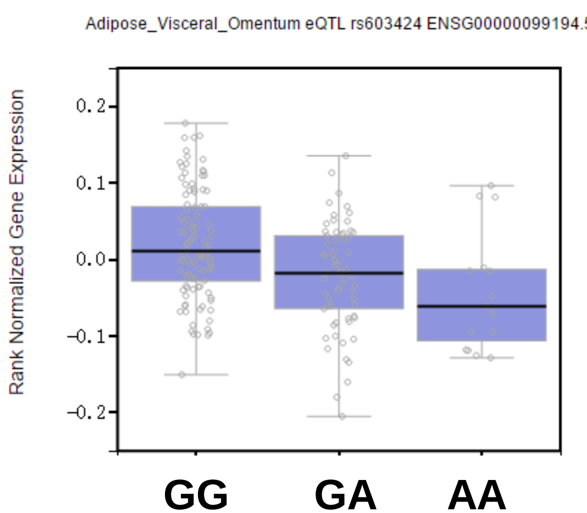
Liver

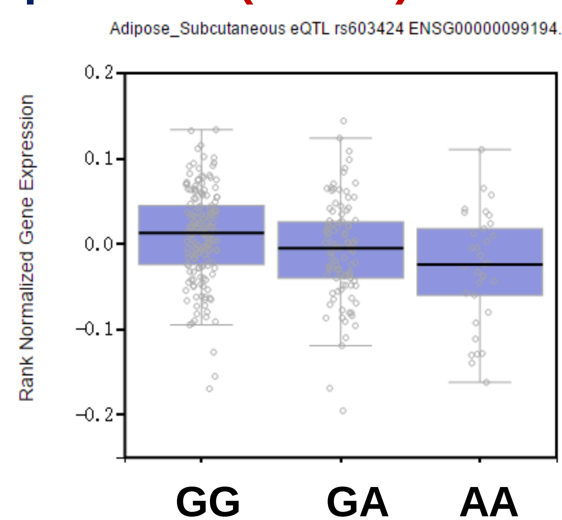
Skeletal Muscle



GTEx Portal

rs603424-A ➡ ↓*SCD* RNA expression (*P*=10^{-6})





16:0

↓ *SCD*

16:1n-7

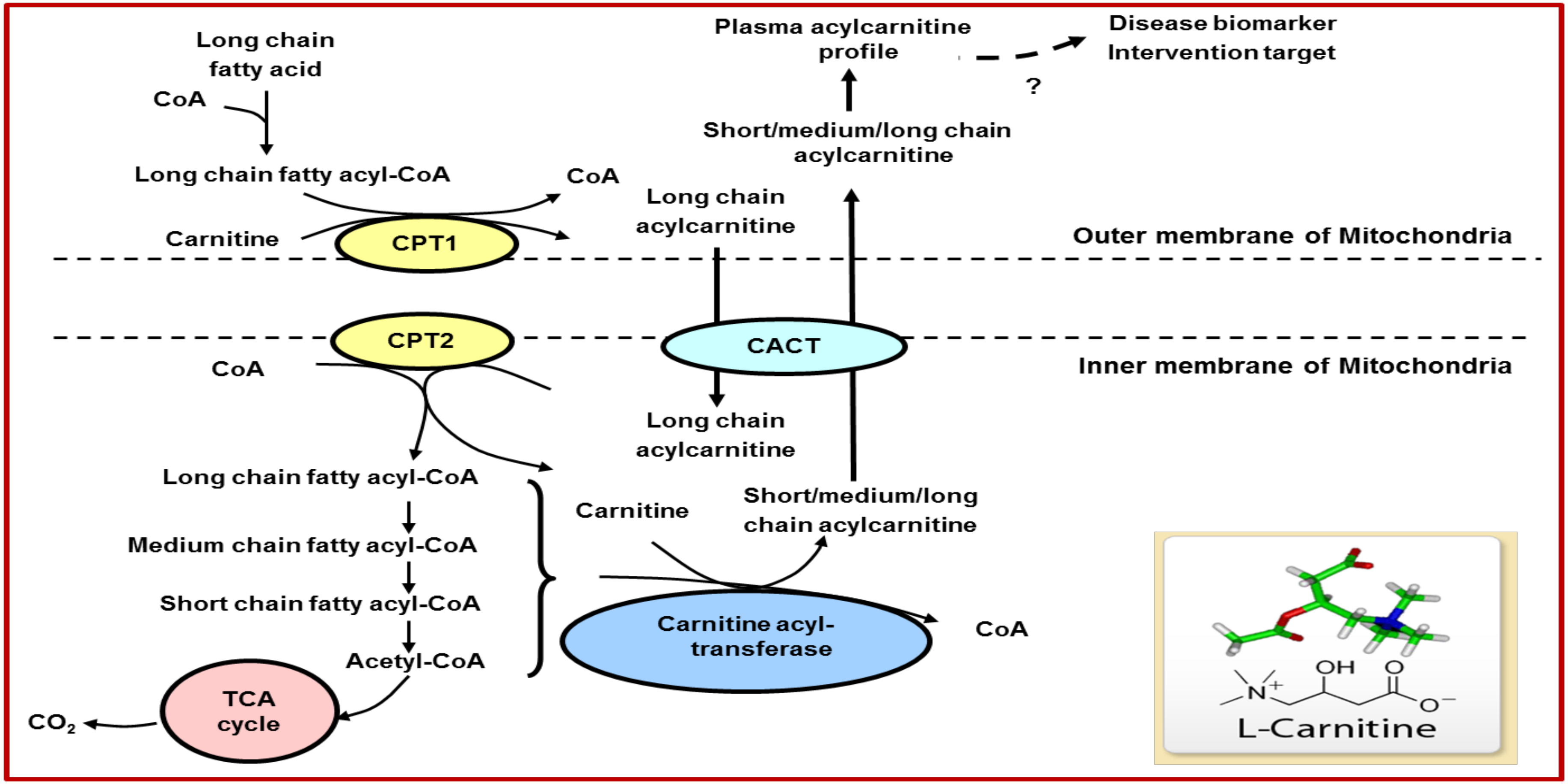
↓

18:1n-7

J Lipid Res (2017)

Acylcarnitines and Fatty Acid Oxidation

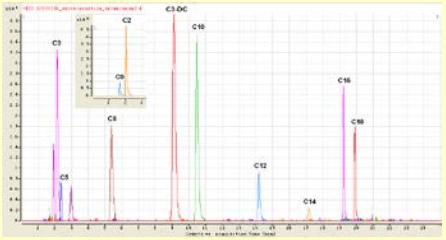
- Acylcarnitines, the intermediates *via* transferring acyl moiety from CoA to L-carnitine
- They transport long-chain (LC) fatty acids to mitochondrial inner membrane
- Hypothesis: ↑ LC-acylcarnitines reflect mitochondria stress and incomplete β-oxidation



Established Acylcarnitines Database

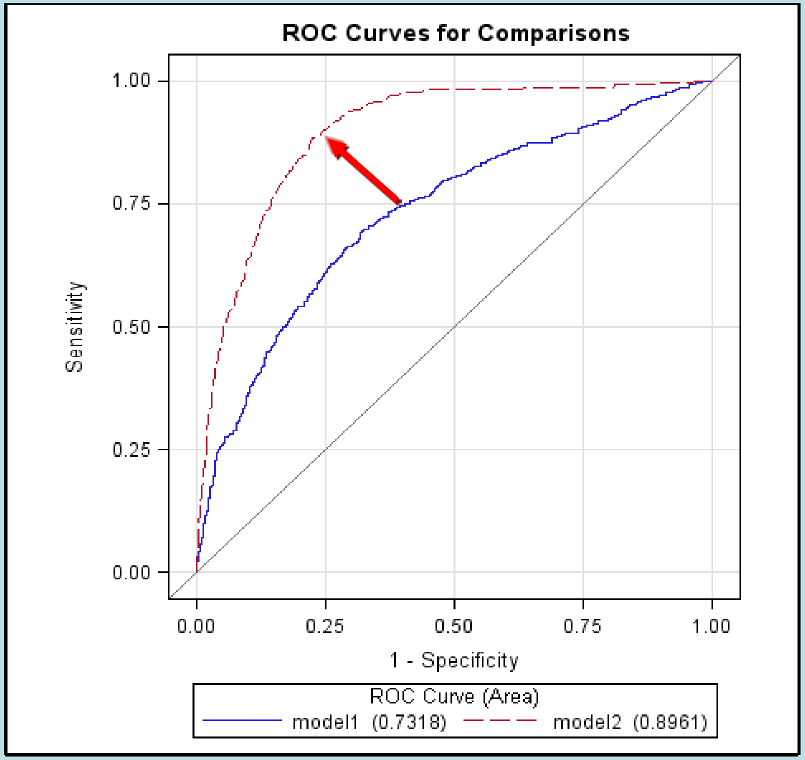
A total of 34 free and acylcarnitines were detected in 2,106 participants completed 6-yr follow-up

- **Free carnitine and precursor**
- **Short-chain acylcarnitine**
- **Medium-chain acylcarnitine**
- **Long-chain acylcarnitine**



LC-MS/MS

Acylcarnitines ↑ Prediction of 6-yr Incident Diabetes



Model 1: conventional model including age, sex, region, residence, smoke, drink, physical activity, family history of diabetes, systolic blood pressure, BMI, glucose & HbA1c, AUC = 0.73;

Model 2: Model 1 + selected acylcarnitines, AUC = 0.90

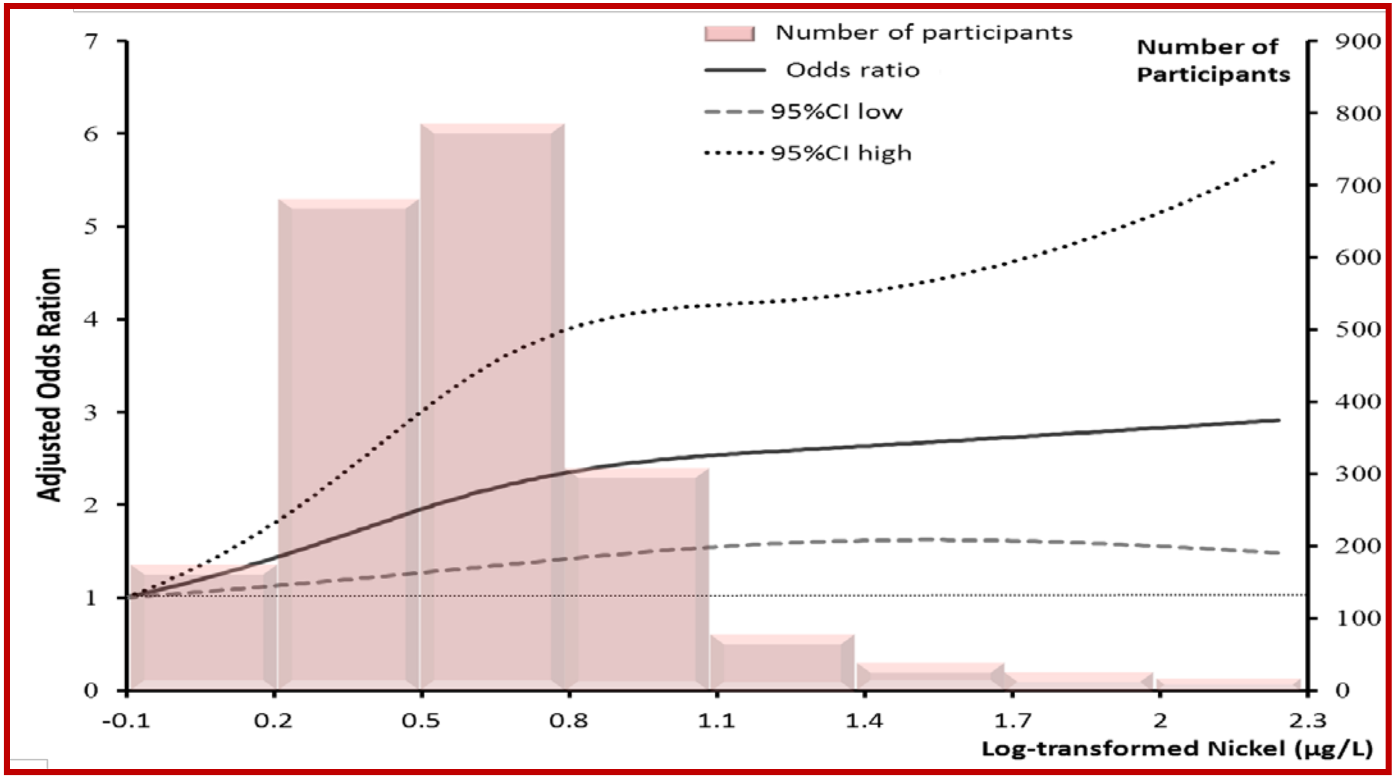
***Diabetes Care* (2016)**

Ionomics and Metabolic Diseases

A total of 33 elements were detected in our 6-yr Follow up samples by ICP-MS:

Al, As, B, Ba, Be, Bi, Ca, Cd, Co, Cr, Cu, Fe, K, Li, Mg, Mn, Na, Ni, P, Pb, Se, Sr, V, Zn, S, Mo, Pd, Re, Sb, Si, Sn, Ti and W

↑ Urinary Nickel Levels were Associated with ↑ T2D Risk



Adjustment including lifestyle factors, BMI, creatinine, C-reactive protein

***Int J Epidemiol* (2014)**

International Journal of Epidemiology, 2015, 248–250
doi: 10.1093/ije/dyv004

Commentary: Environmental chemicals and diabetes: which ones are we missing?

Chin-Chi Kuo[1,2,3,4] and Ana Navas-Acien[1,2,3]*

[1]Department of Epidemiology, and [2]Department of Environmental Health Sciences, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA, [3]Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins Medical Institutions, Baltimore, MD, USA and [4]Kidney Institute and Division of Nephrology, Department of Internal Medicine, China Medical University Hospital and College of Medicine, Taichung, Taiwan

*Corresponding author: 615 N Wolfe Street, Room W7513D, Baltimore, MD 21205. E-mail: anavas@jhu.edu

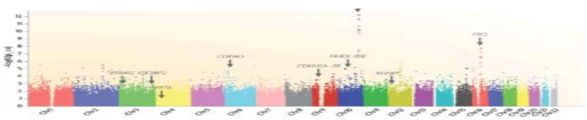
“ With the publication of the study by Liu et al., nickel appears as a potential new chemical that was missing in our list of environmental chemicals that may be related to diabetes. ”

International Journal of Epidemelogy

What we have found so far?

Genetic Factors

- Found multiple obesity and T2D associated genetic variants
- Different gene structures cannot explain ↑susceptibility



Environmental Factors

- Diet and nutrient biomarkers
  - DHA, Trans-18:1 (Dairy) Trans-18:2 and DNL fatty acids
  - Ferritin, vitamin D, soy protein
- Lifestyle factors
  - Physical activity
  - Depression
  - Alcohol
- Pollutants

- *FADS1* (PUFA)
- *TMPRSS6* (Ferritin)
- *GC, NADSYN1 DHCR7* (Vitamin D)

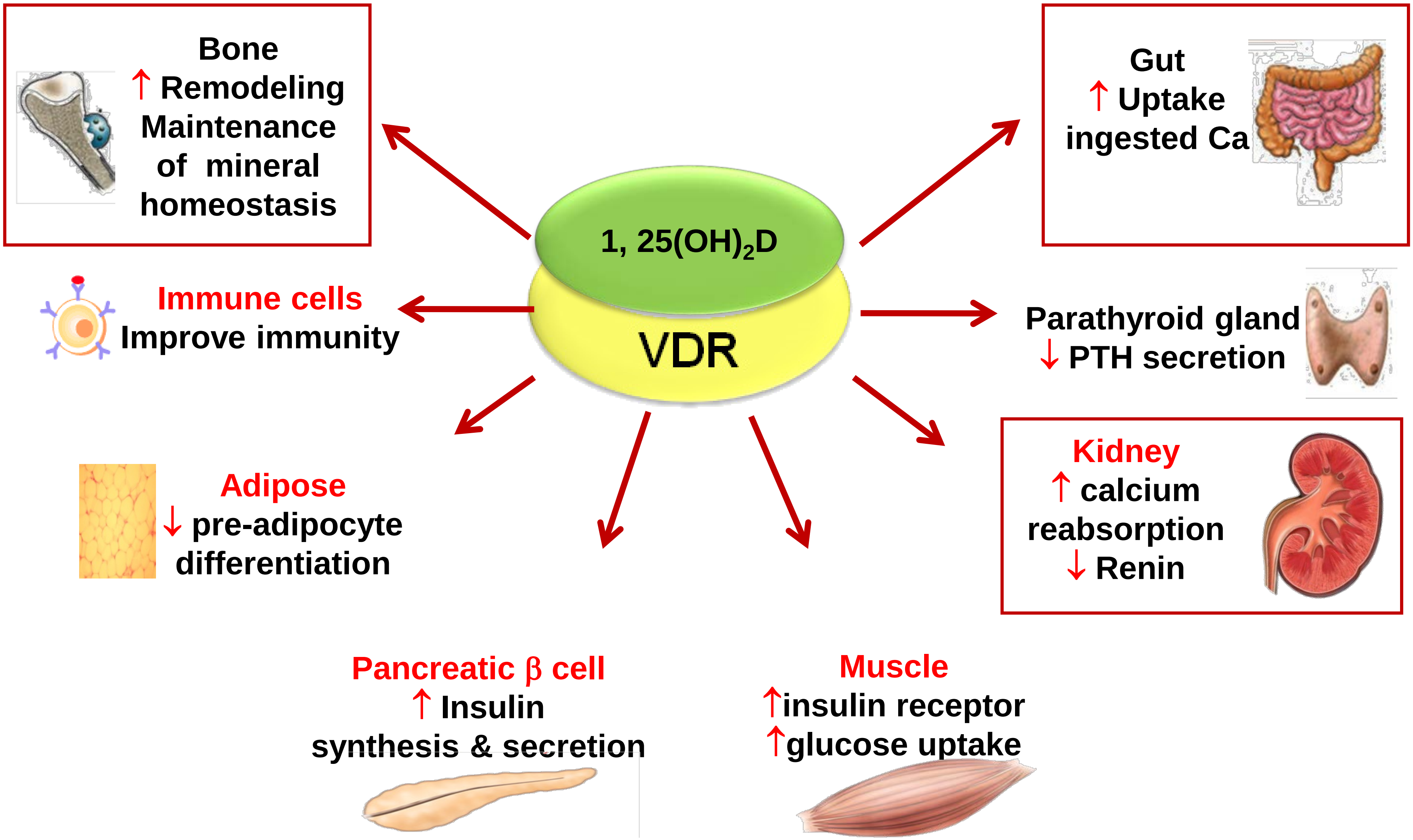
- CRP, IL6
- RBP4
- LBP
- Adiponectin
- Trunk fat

Suggesting potential roles of omics-based biomarkers in determining nutritional status and predicting metabolic diseases

Outline

- Background
- Finding from our studies
  - Observational studies
  - Intervention trials
- Currently ongoing studies

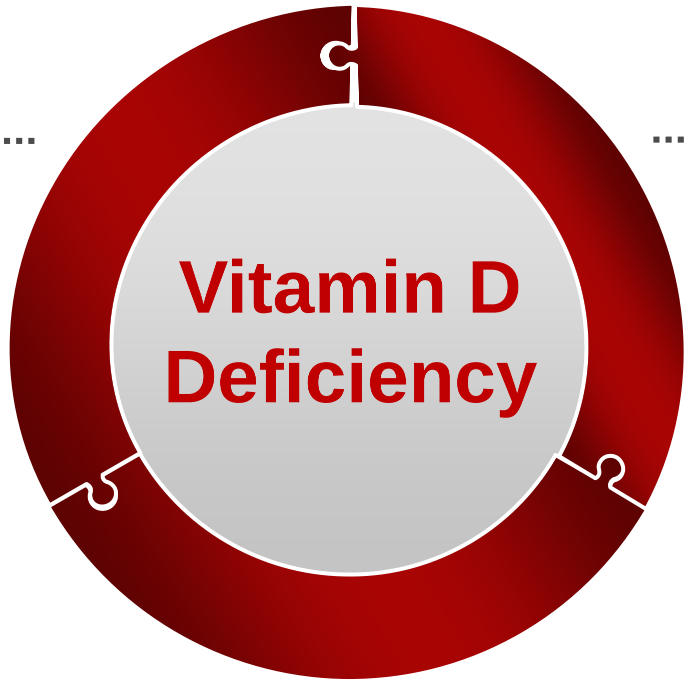
Roles of Vitamin D on Health



Modifying Factors for Vitamin D Status

Environmental factors

- sunlight exposure (season, latitude...)
- dietary intake
- vitamin D supplement
- …



Physiological factors

- age
- obesity
- skin pigment
- …

Genetic factors

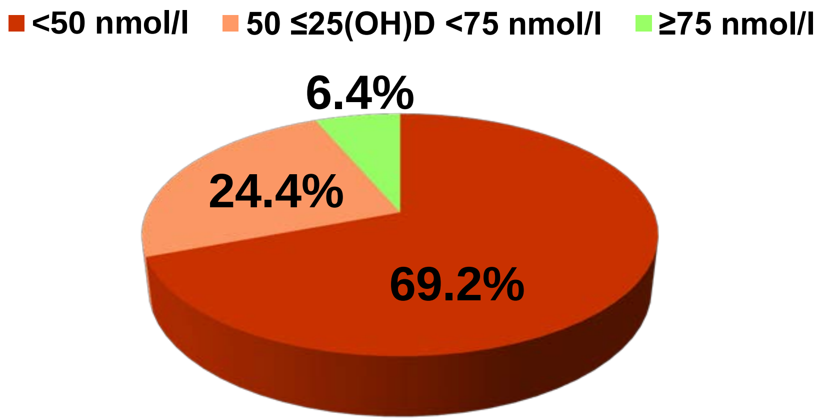
- *GC*

Few studies have systematically evaluated effect of genetic and non-genetic factors on vitamin D response

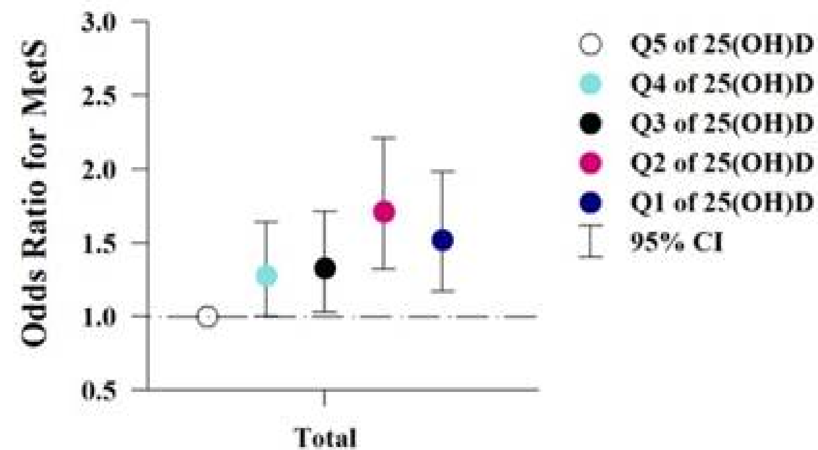
Vitamin D and Metabolic Disorders – Our data

A population-based study (n=3280, aged 50-70 yrs)

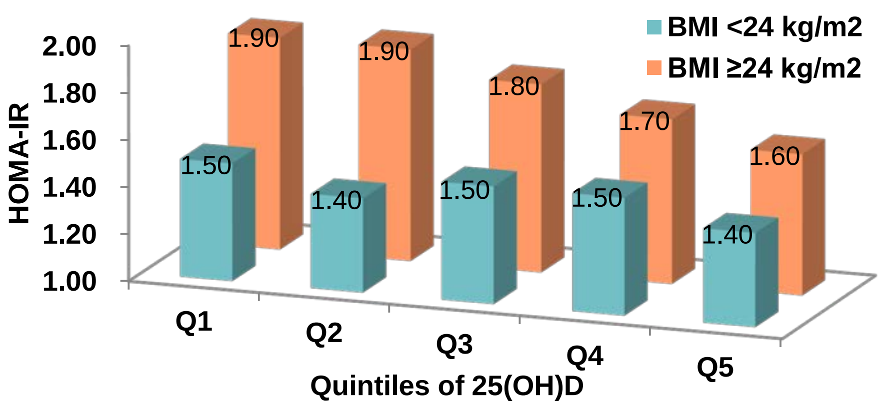
Plasma 25(OH)D Profile



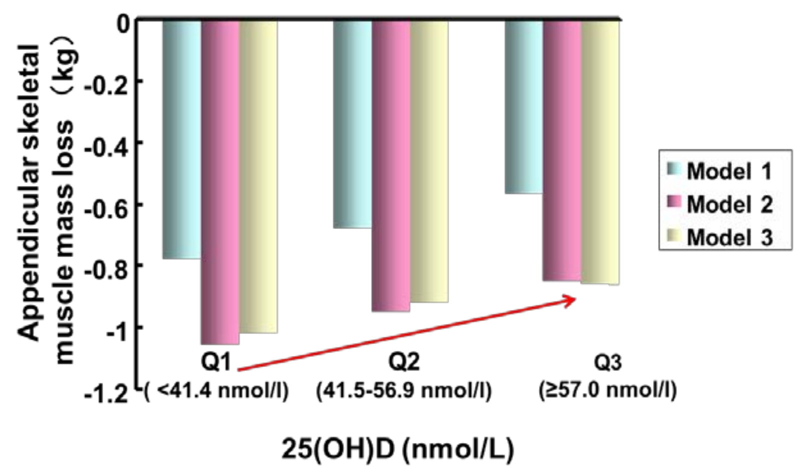
↓ 25(OH)D ↑ Metabolic Syndrome



↓ 25(OH)D ↑ Insulin Resistance

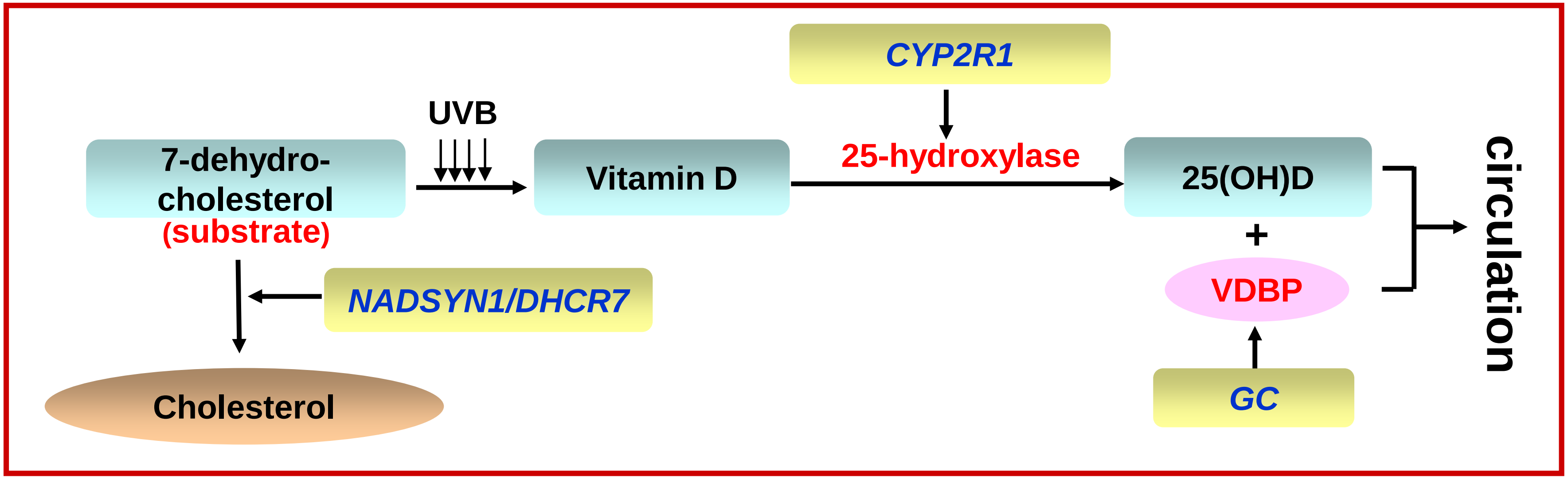


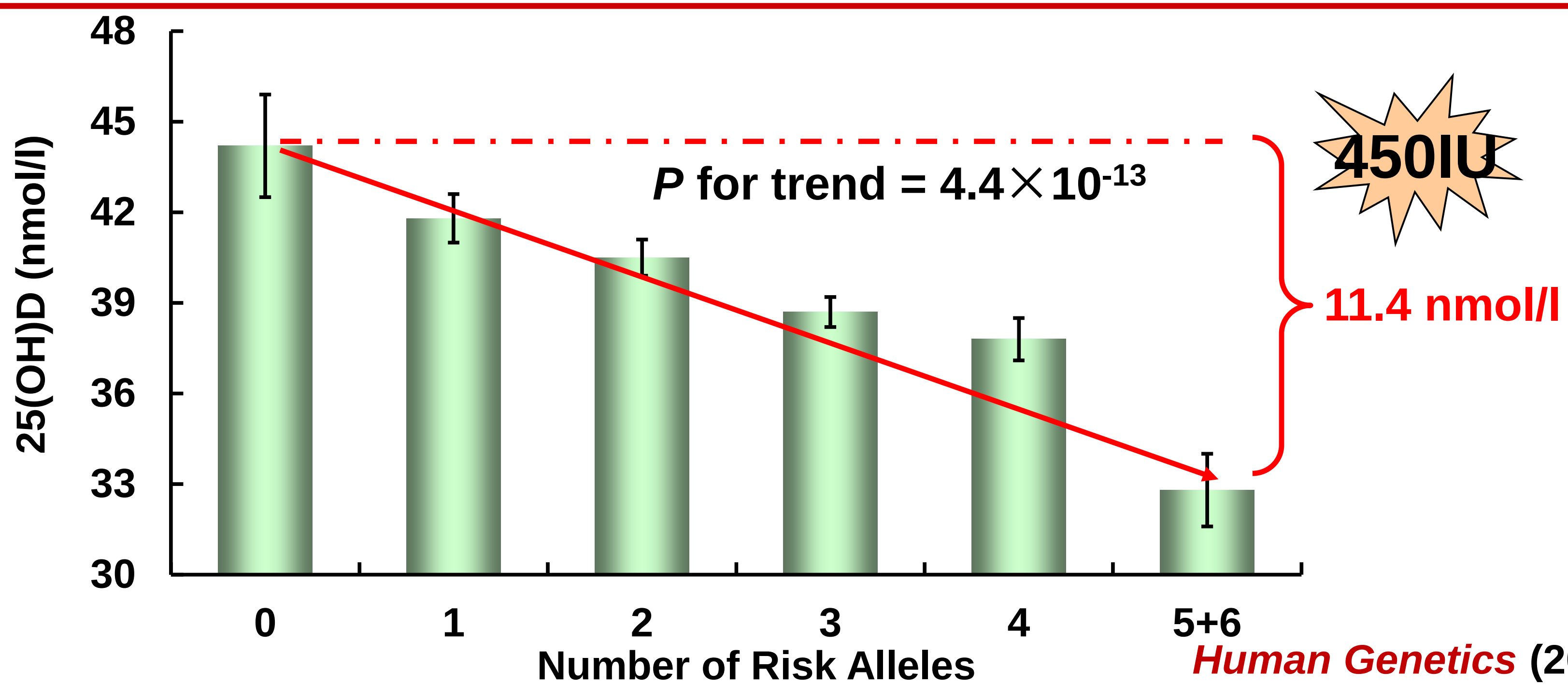
↓ 25(OH)D ↑6yr Muscle Mass Loss



Diabetes Care (2009) , *J Acad Nutr Diet* (2014)

Vitamin D related Genetic Polymorphisms –Our data





Human Genetics (2012)

Study Design for Vitamin D_3 Trials

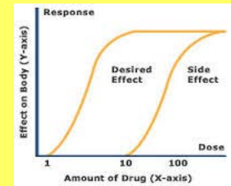
Randomized Double-blind Placebo-controlled trials

Trial I

75 Subjects

25(OH)D < 50 nmol/l

$VitD_3$ doses (IU/d)
- 0
- 400 Chinese RDA
- 800
- 1200
- 2000 Chinese UL



- Dose response
- Adverse effect

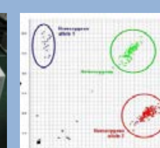
Dose — Time frame

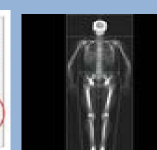
Trial II

400 Subjects

25(OH)D < 50 nmol/l

$VitD_3$ doses (IU/d)
- 0
- 2000 IU

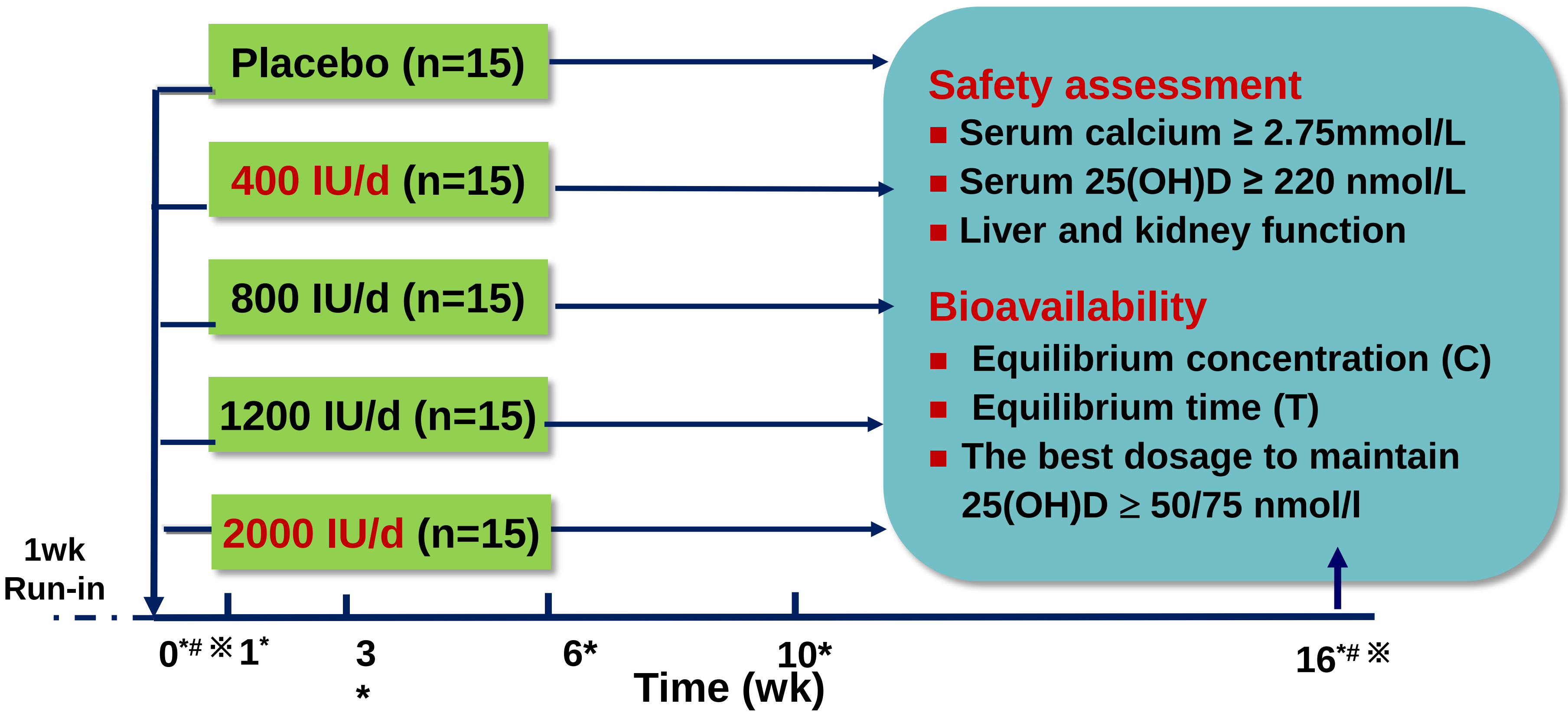




- VitD bioavailability
- Effects of genetic factor,
- VitD binding protein
- BMI, sex…

Trial I: A Dose–Response Study with $VitD_3$

- A 5-arm randomized, placebo-controlled trial
- 20-45 yrs with 25(OH)D <50nmol/l

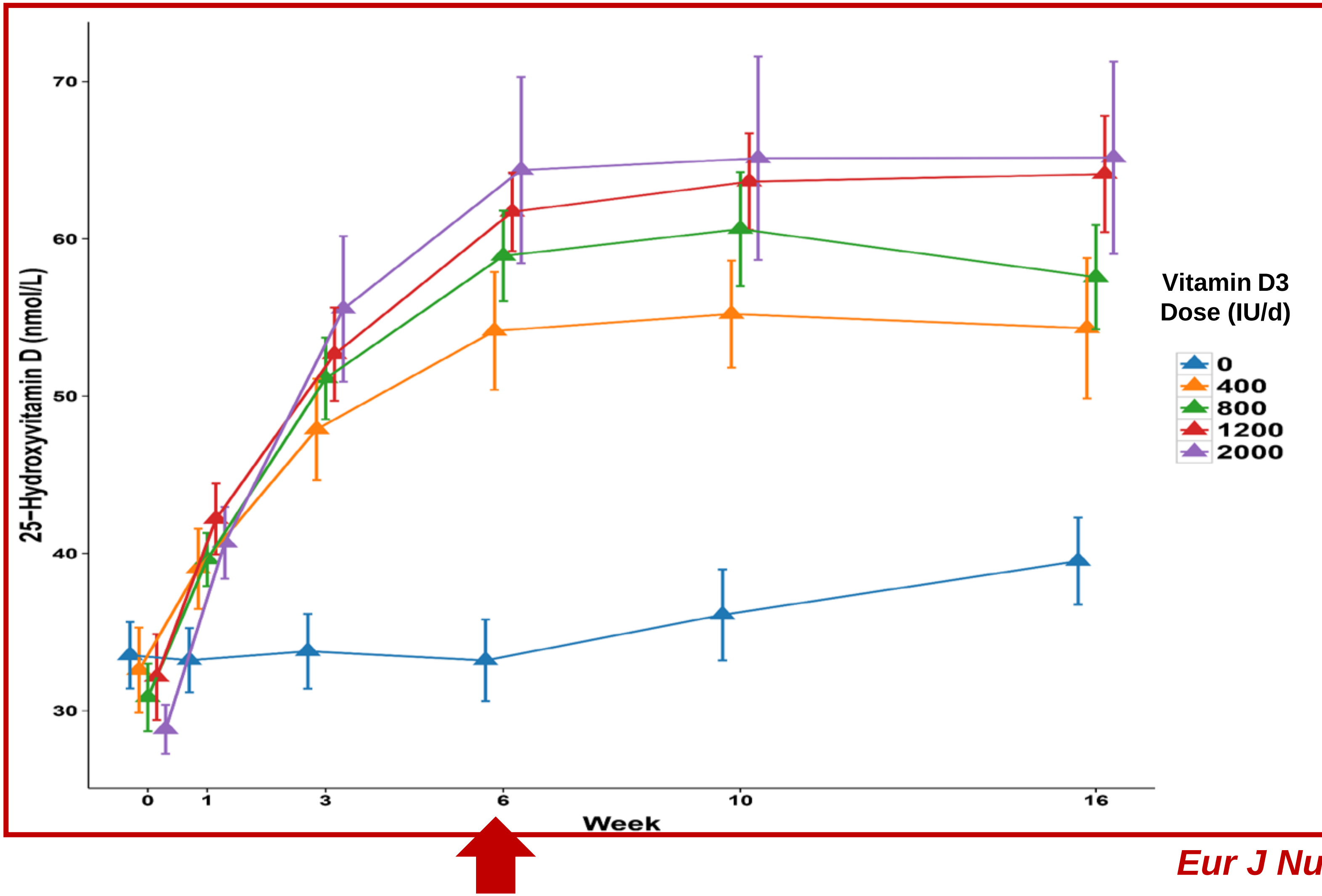


* Blood and urine collection # physical examination ※ Questionnaires

A 3-day food record and information of sunlight exposure and supplement intake were collected every 4 wks

Trial I: Dose–Response

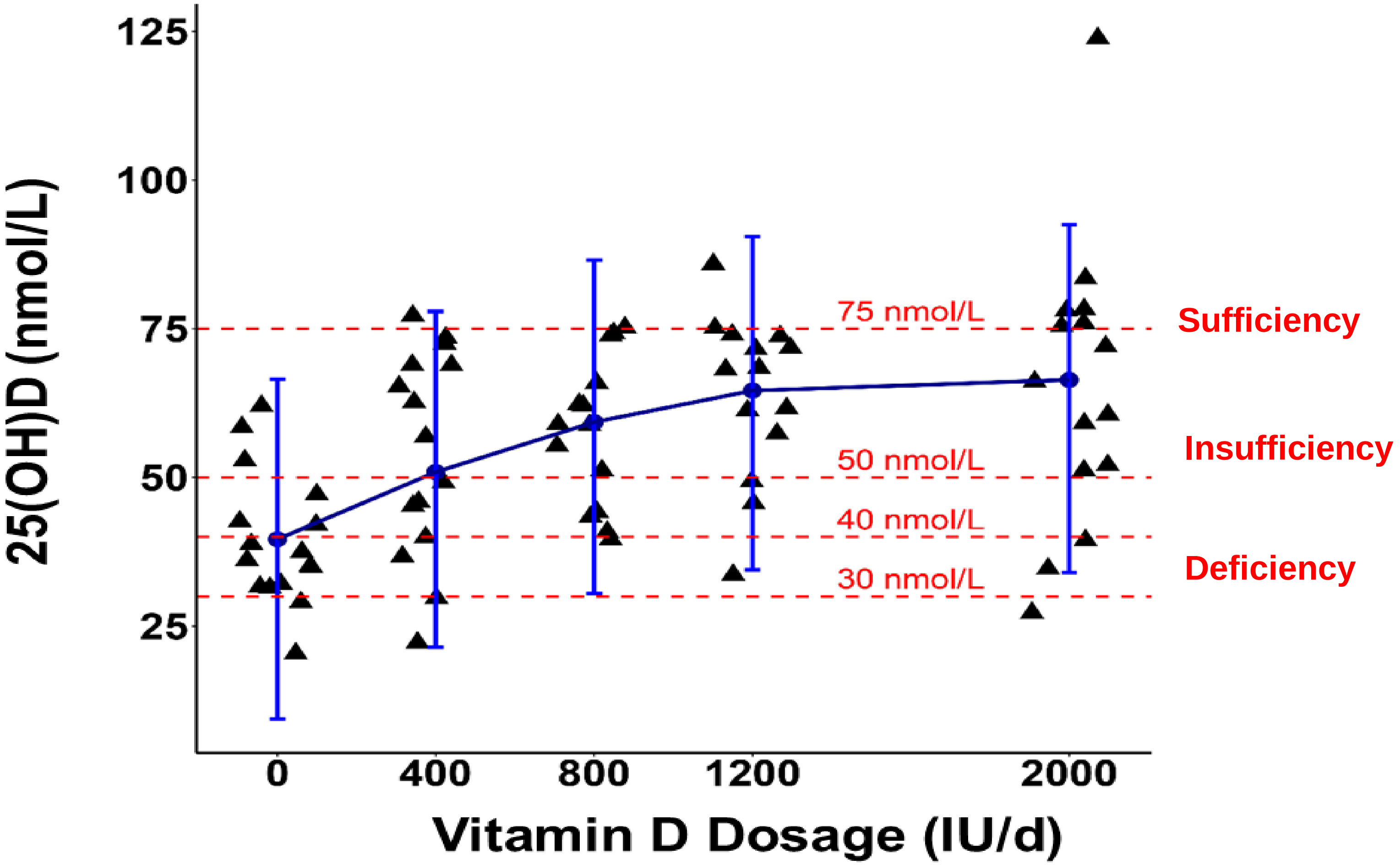
Serum 25(OH)D in all the doses (400-2000IU) of VitD$_3$ reached a plateau at about week 6



Eur J Nutr (2015)

Trial I: Efficacy of VitD$_3$ Intervention

2000 IU/d VitD$_3$ for 16 weeks ↓80% deficiency without major adverse reactions

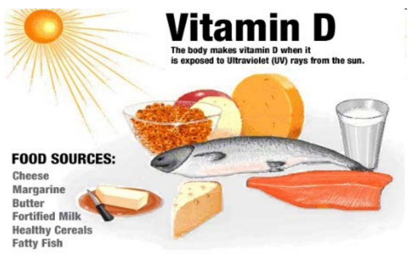


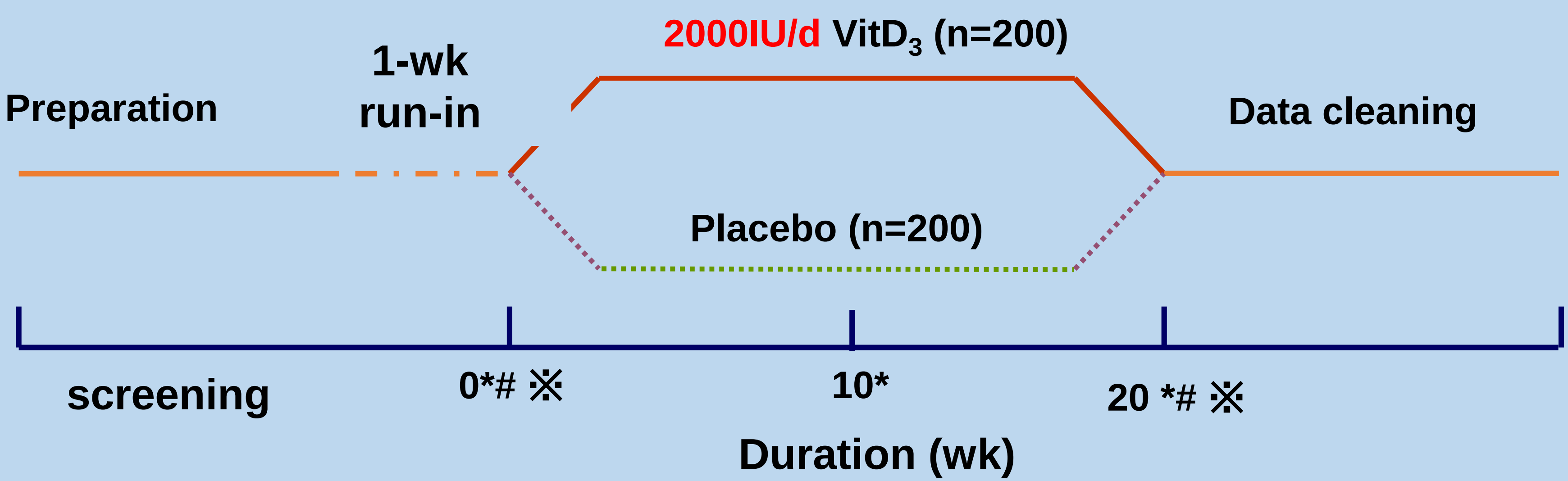
Eur J Nutr (2015)

Trial II: Study Design

A double-blind randomized, controlled trial

- 20-40 yrs, 50% men
- 25(OH)D <50nmol/L
- BMI: 18.5-28 kg/m^2





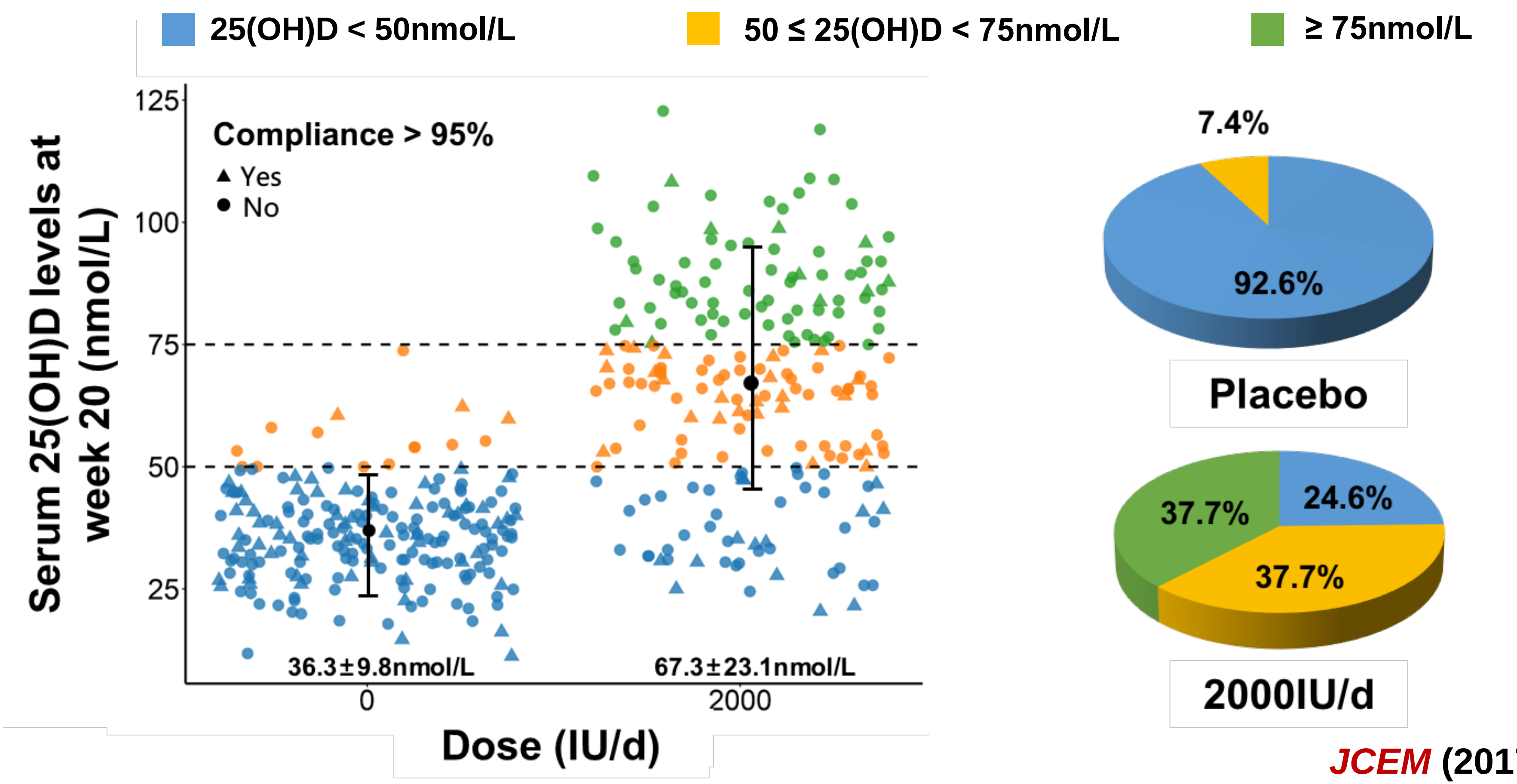
* Blood and urine collection # physical examination ※ Questionnaires

A 3-d food record and information of sunlight exposure and supplement intake were collected at week 0, 10 and 20

Trial II: Changes of 25(OH)D Levels

Supplemented 2000IU/d VitD for 20 weeks:

- **Net increase of 25(OH)D was 30.6±1.7nmol/L**
- **There were 25% participants with uncorrected deficiency**



JCEM (2017)

Vitamin D Bioavailability

"Vitamin D Paradox"?

African Americans have a lower total serum 25(OH)D but superior bone health

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Vitamin D–Binding Protein and Vitamin D Status of Black Americans and White Americans

Community-dwelling black Americans, as compared with whites, had low levels of total 25-hydroxyvitamin D and vitamin D–binding protein, resulting in similar concentrations of estimated bioavailable 25-hydroxyvitamin D. Racial differences in the prevalence of common genetic polymorphisms provide a likely explanation for this observation. (Funded by the National Institute on Aging and others.)

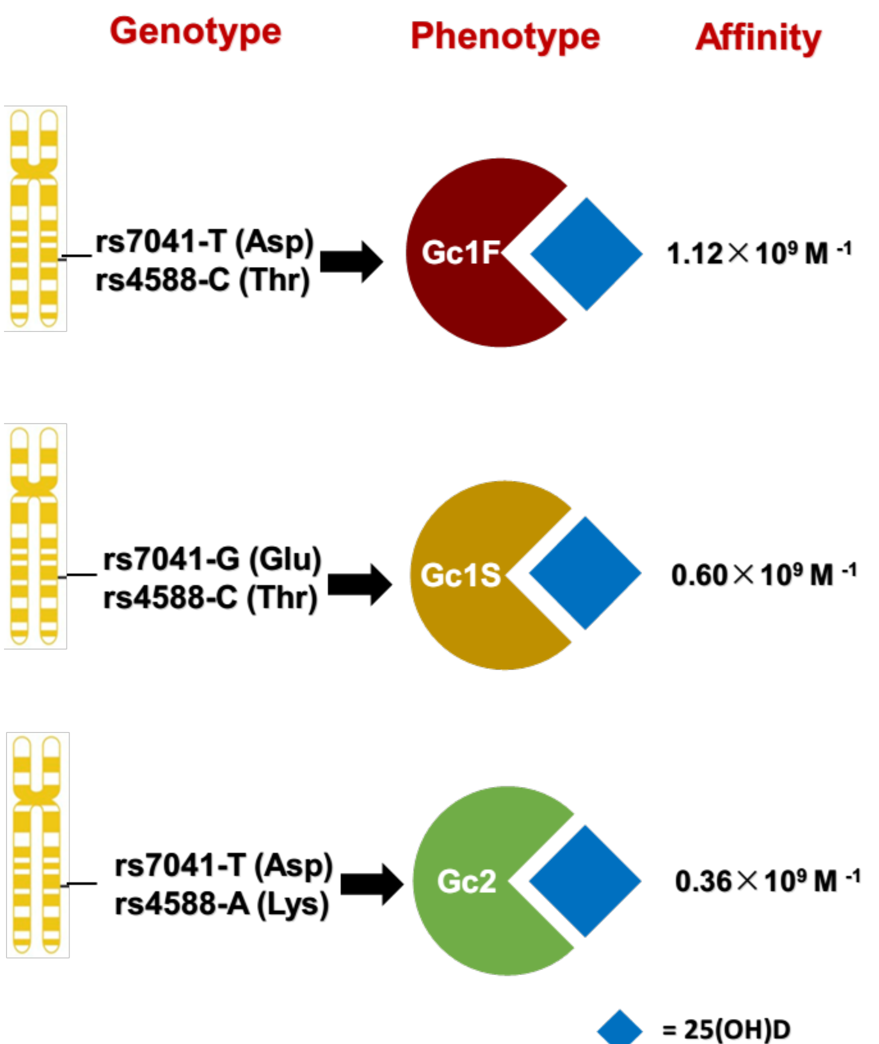
Total 25(OH)D: VDBP-bound (85-90%) + Albumin-bound (10-15%) + Free (< 1%)

Bioavailable 25(OH)D ($25[OH]D_{Bio}$)

Cross-sectional studies suggested that associations of $25(OH)D_{Bio}$ with serum calcium, PTH or BMD status were stronger than those associations of 25(OH)D

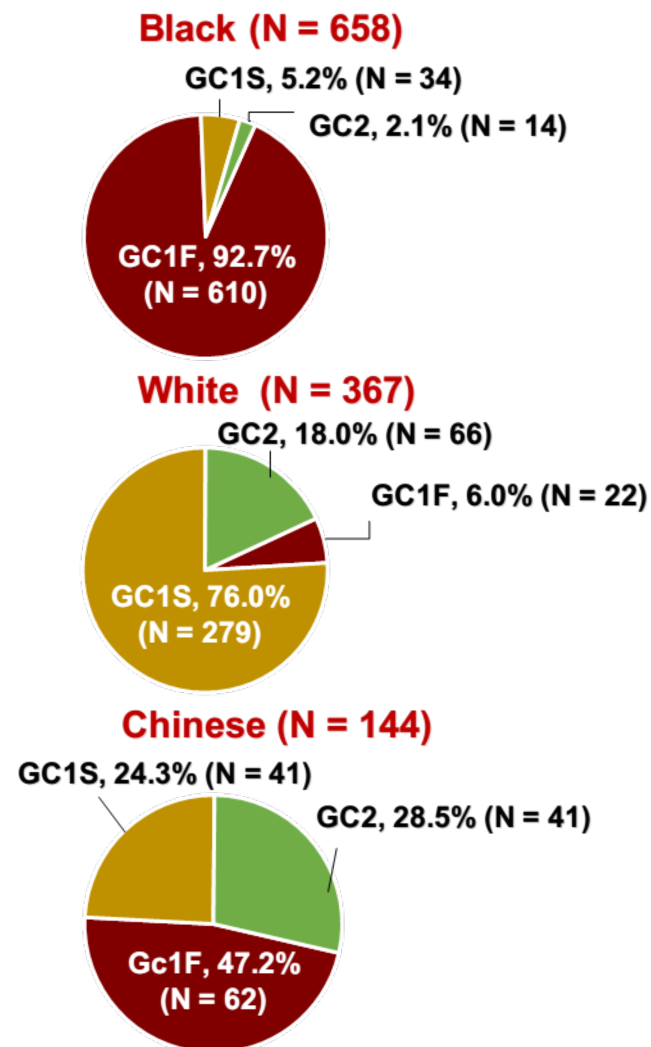
GC Polymorphisms and VDBP Isoforms

SNPs in *GC* produce VDBP variants with different affinities



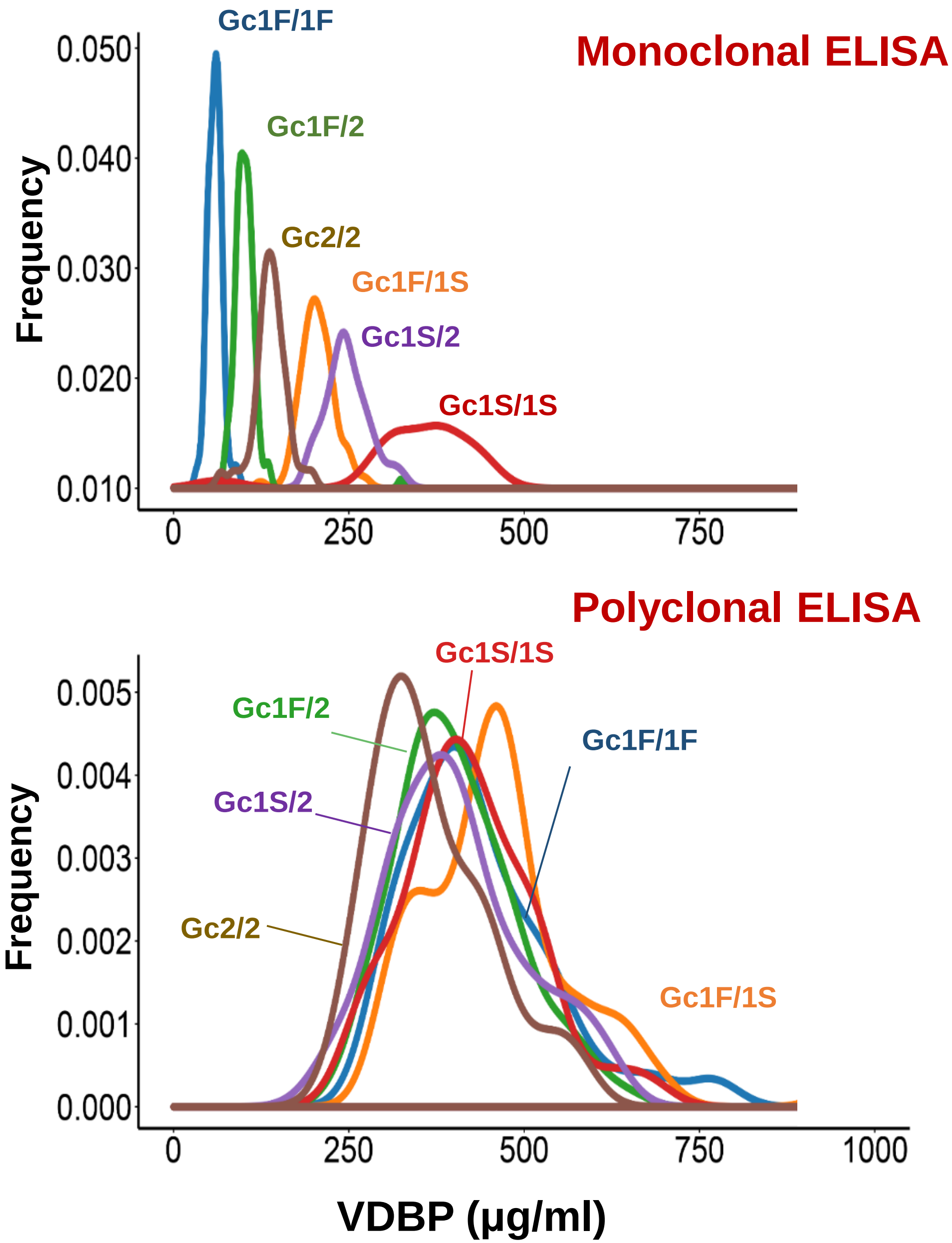
Adapted from Powe NEJM (2013) *Hum Genet* (1993)

Ethnic difference in homozygotes distribution



JCEM (2017)

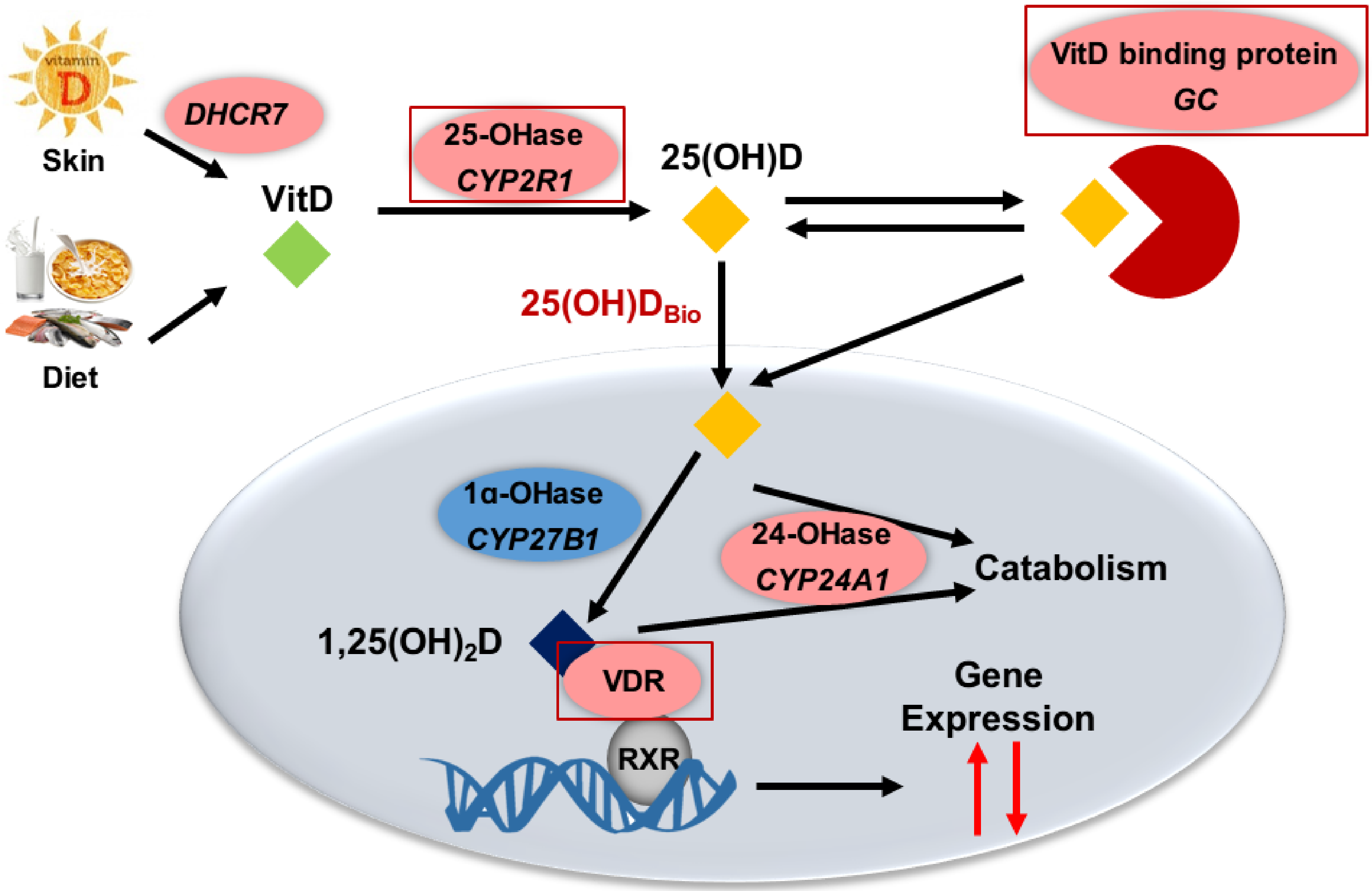
VDBP Measured by Mono- and Polyclonal ELISAs



- **Monoclonal ELISA:** **165.3±90.4μg/ml**
- **Polyclonal ELISA** **418.7±99.0μg/ml (*P* < 0.001)**
- **The polyclonal ELISA is a prefer method to assess VDBP and 25(OH)D_{Bio} for populations with relatively higher Gc1F/1F frequency like Blacks and Chinese**

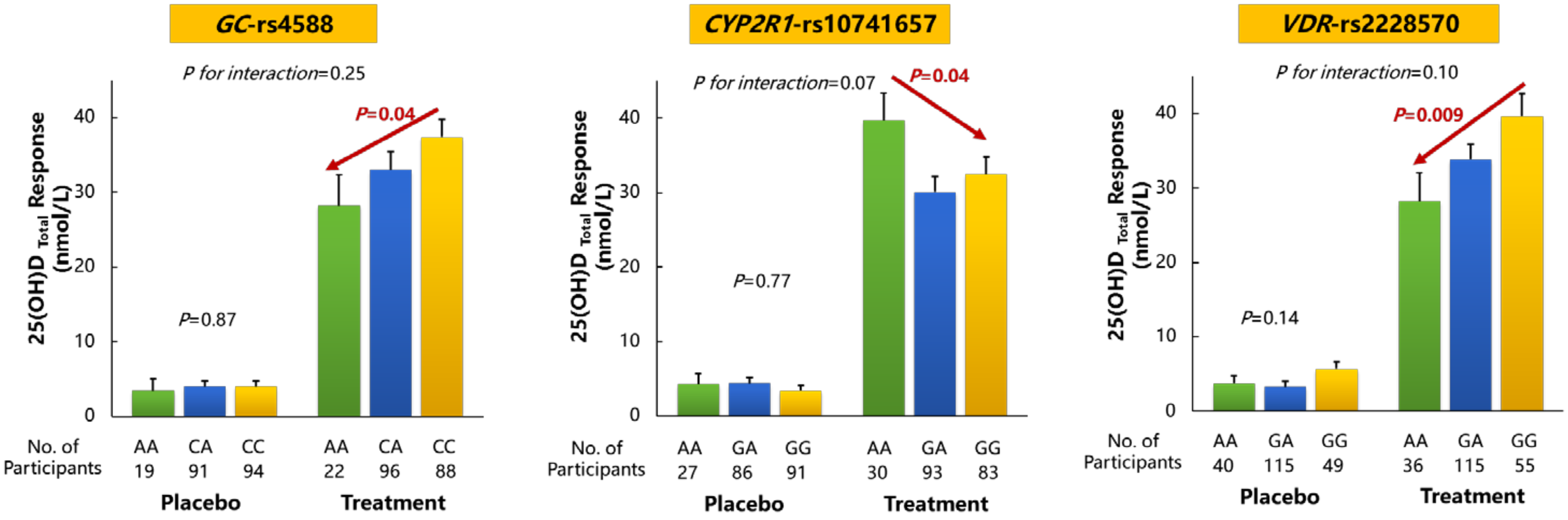
JCEM **(2017)**

Vitamin D Metabolism Pathway



Trial II: Gene Variants and 25(OH)D Responses

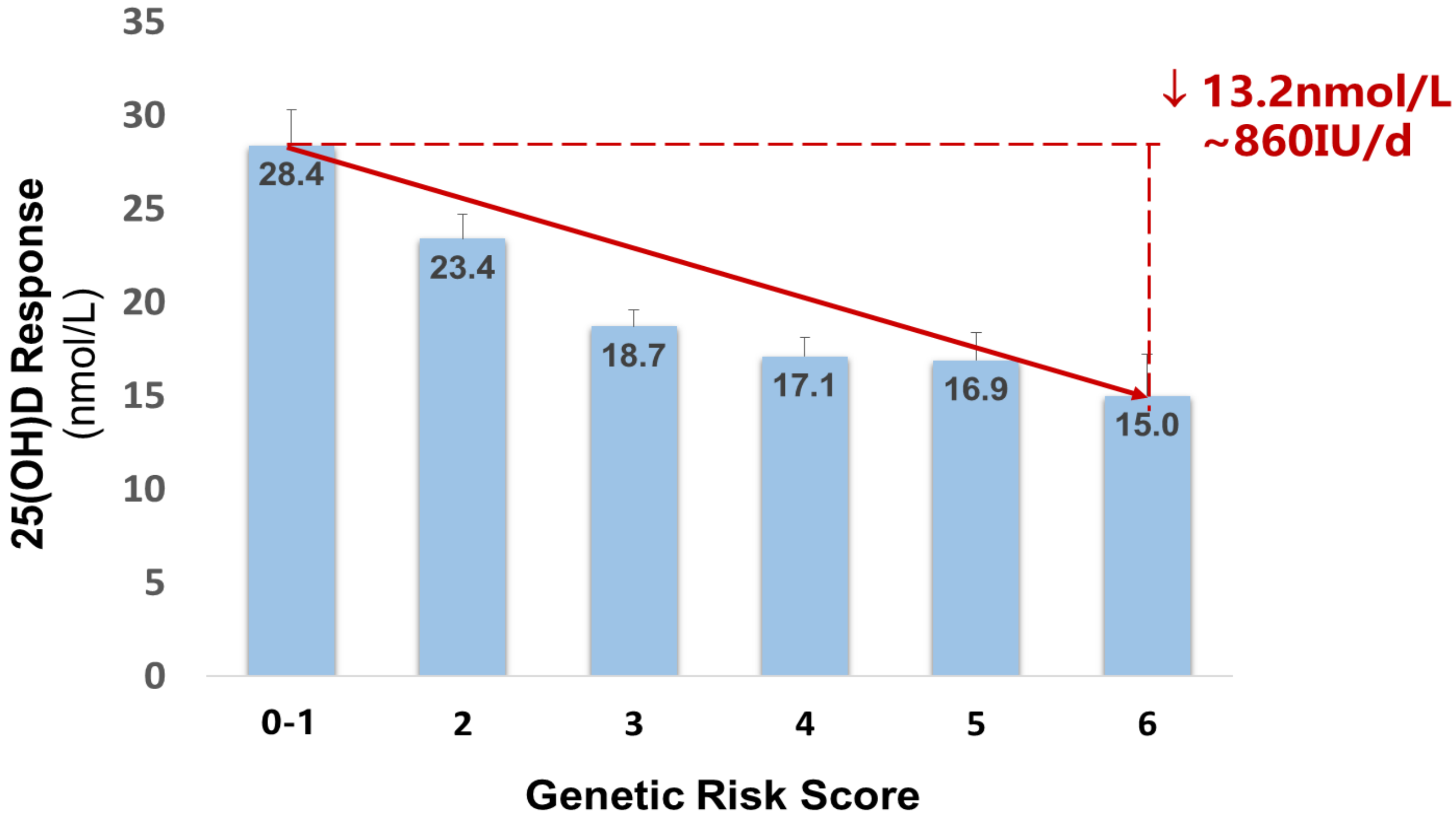
***GC*-rs4588 A, *CYP2R1*-rs10741657 G and *VDR*-rs2228570 A alleles were associated with ↓ 25(OH)D responses**



JCEM (2017)

Trial II: GRS×Treatment Interaction and 25(OH)D Responses

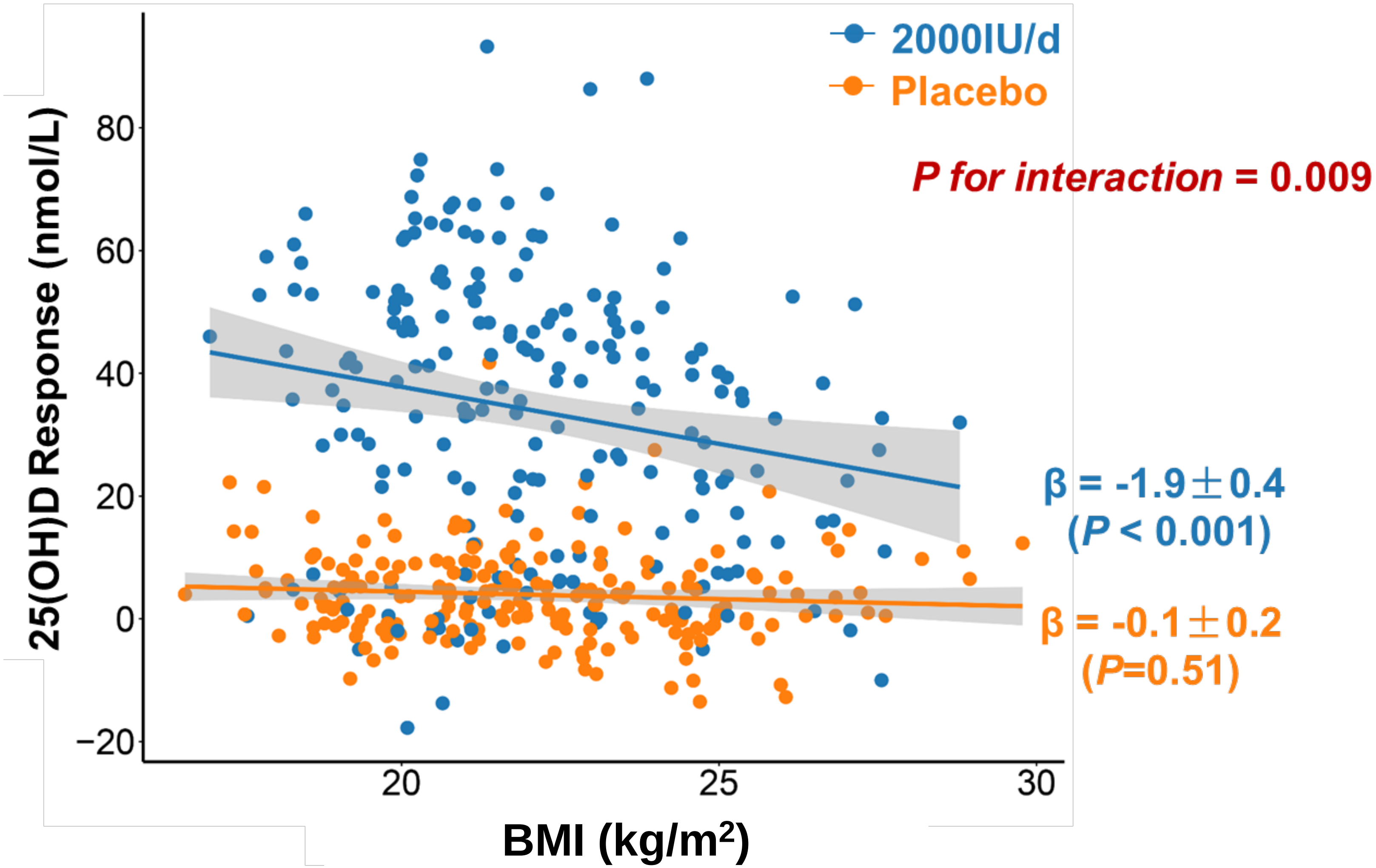
- **Genetic risk score** (GRS) = rs4588-A + rs10741657-G + rs2228570-A
- GRS×Treatment interaction ($P_{for\ interaction}$ = 0.04)



JCEM (2017)

Trial II: BMI and 25(OH)D Responses

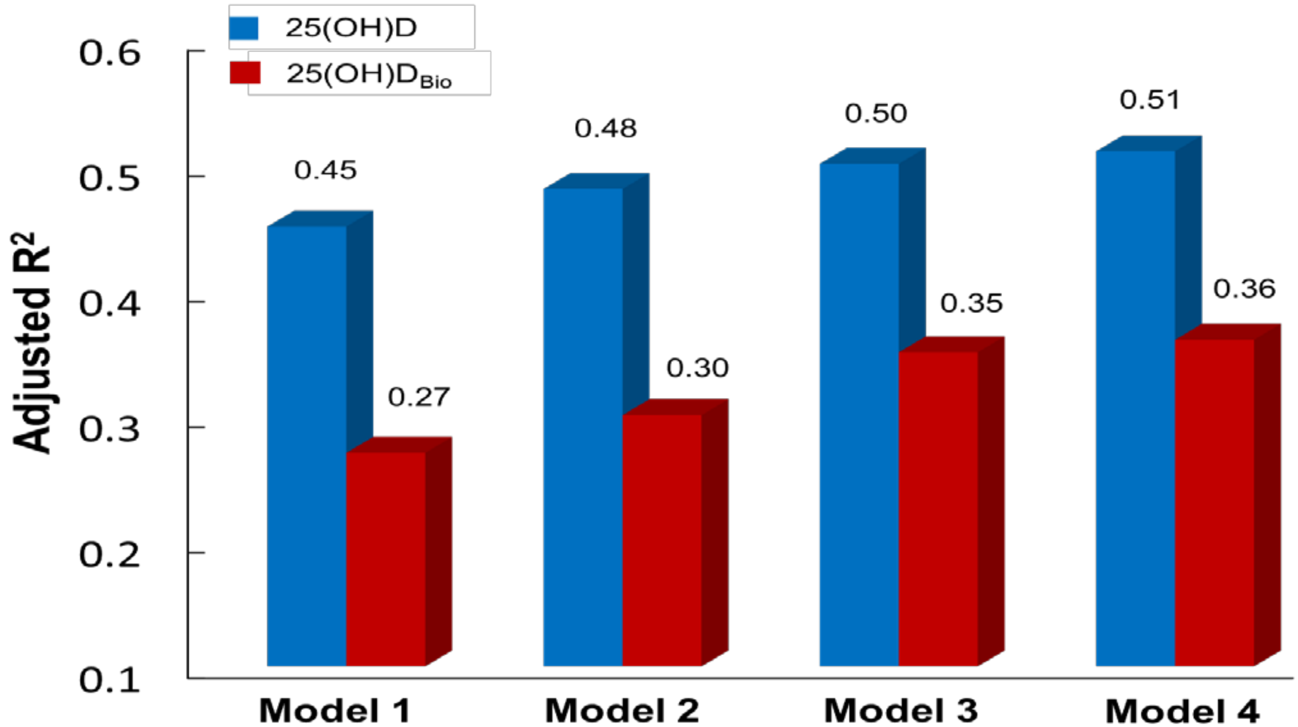
↑ BMI per unit → ↓25(OH)D responses by 1.9nmol/L



JCEM (2017)

Trial II: Effects of Genetic and Non-genetic Factors

Genetic factors showed stronger impacts than non-genetic factors on 25(OH)D and 25(OH)D_{Bio} responses

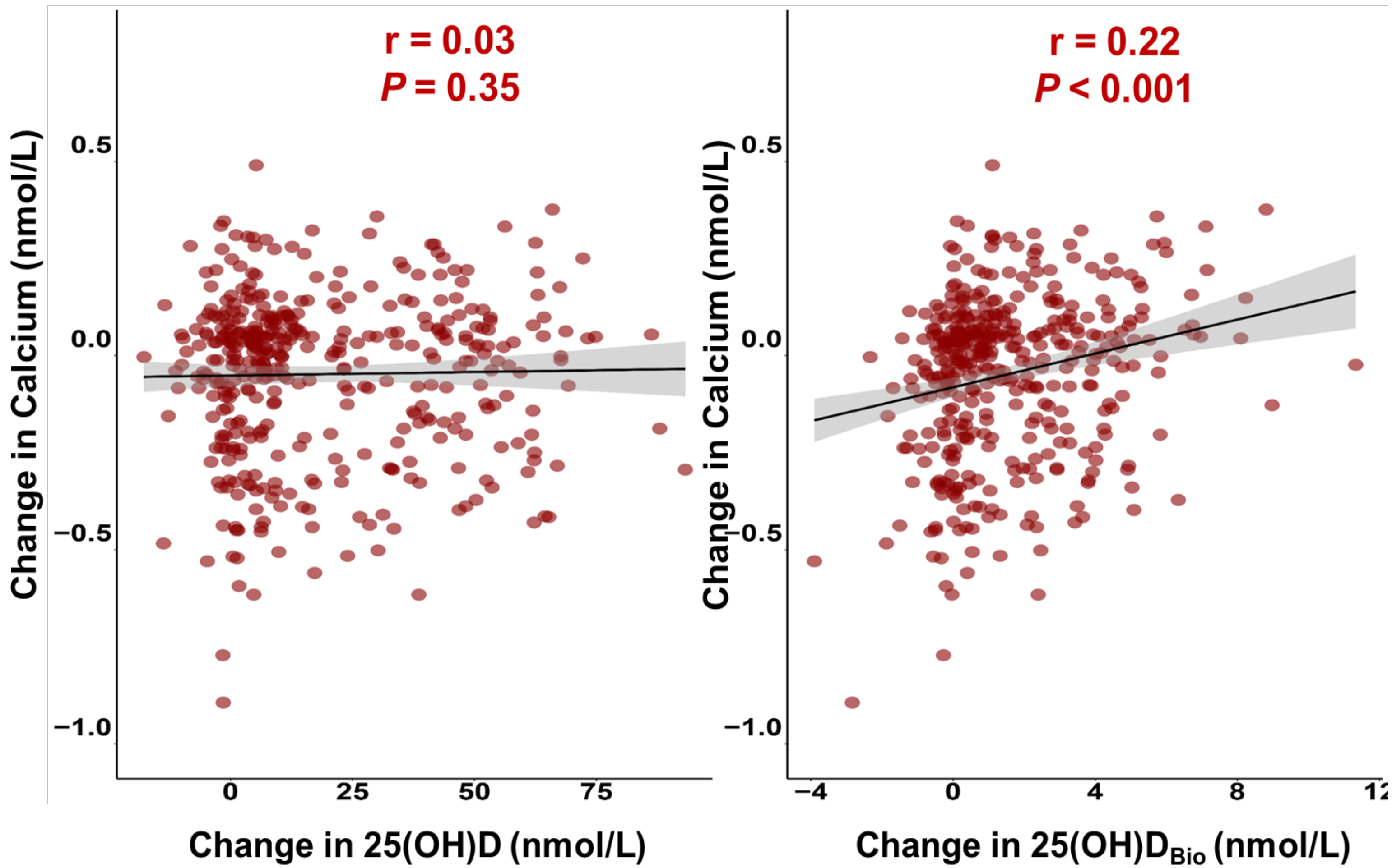


Model 1: dose
Model 2: model 1 + non-genetic factors (basal values, gender, BMI)
Model 3: model 1 + genetic factors (genetic risk score)
Model 4: model 2 + model 3

JCEM (2017)

Trial II: Serum Calcium and 25(OH)D

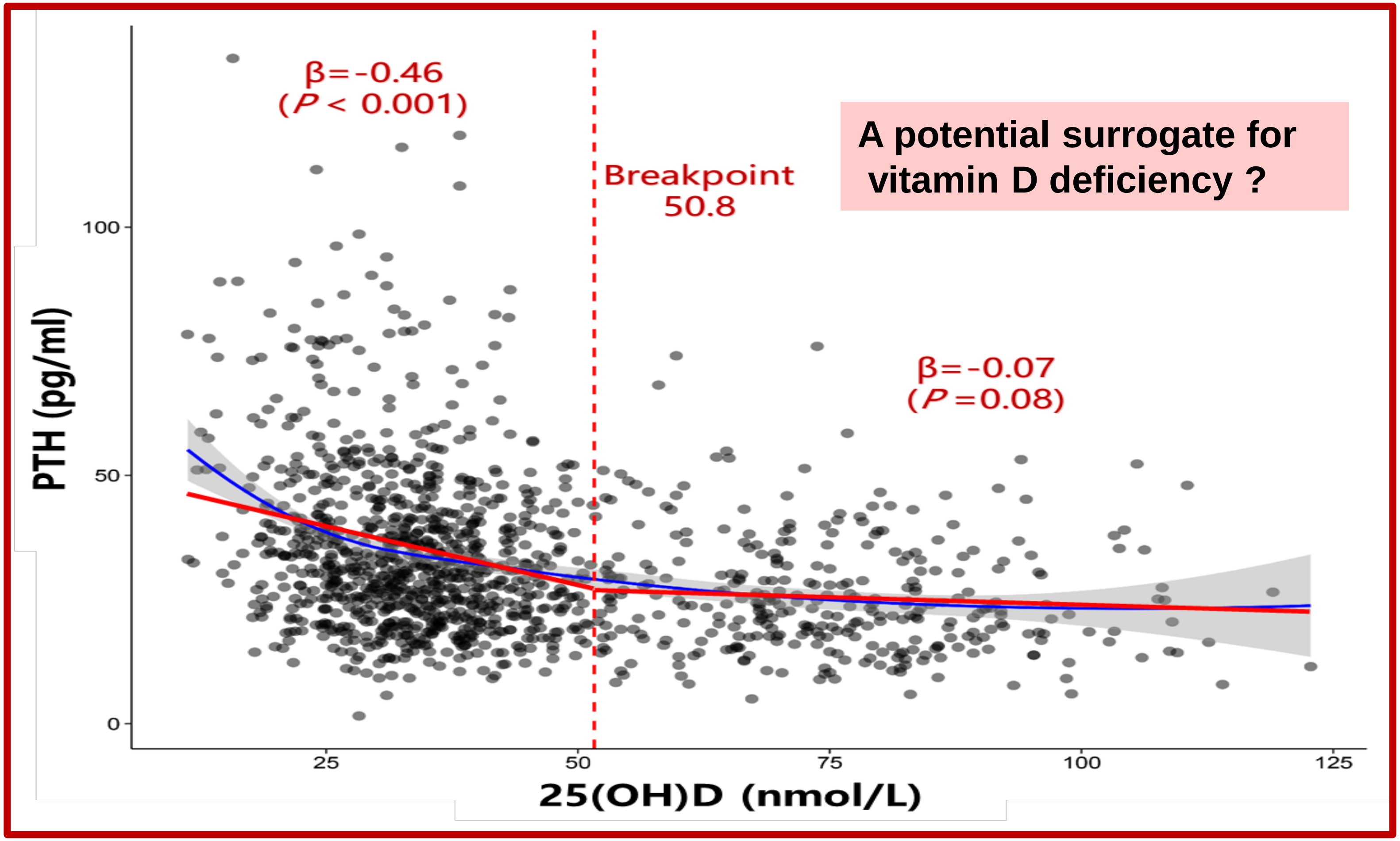
Only change of $25(OH)D_{Bio}$ was positively associated with change of serum calcium



JCEM (2017)

Trial II: 25(OH)D Threshold for PTH Suppression

Serum PTH level was maximally suppressed when 25(OH)D≥50.8 nmol/L



JCEM (2017)

Summary

- Daily supplemented 2000 IU VitD$_3$ $\uparrow$ total and bioavailable 25(OH)D levels, but still left uncorrected deficiency
- 25(OH)D$_{Bio}$ might provide additional information reflecting vitamin

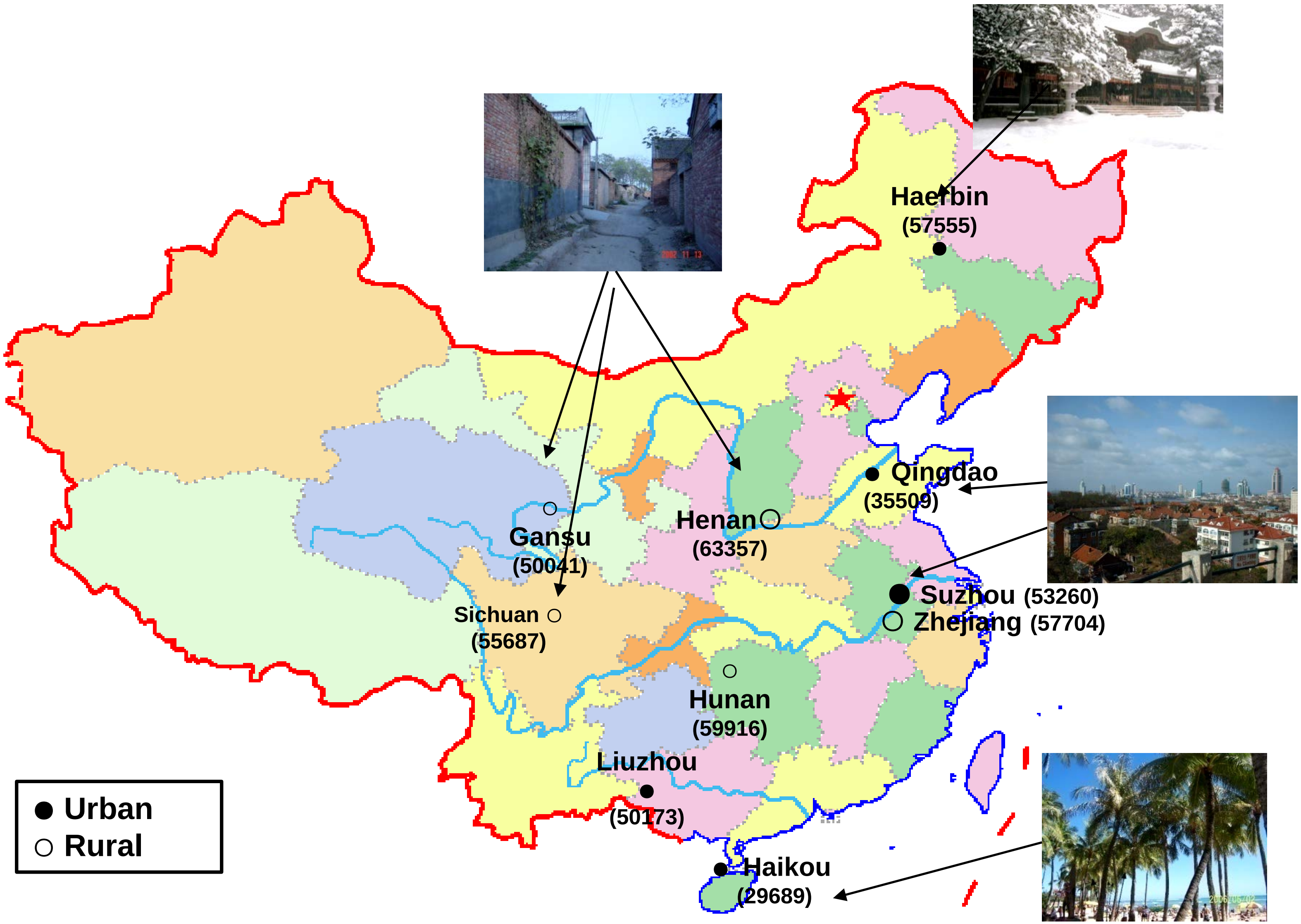
When waiting for more studies with bone and cardiovascular outcomes,

it is important to take trans-ethnic and interpersonal variations of genetic and non-genetic factors into account for precise vitamin D recommendation and assessment

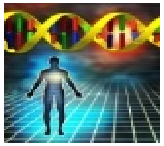
Outline

- Background
- Finding from our studies
  - Observational studies
  - Intervention trials
- **Currently ongoing studies**

Measuring Fatty Acids (N= 10,000) from China Kadoorie Biobank Study (n=0.5 million, 10 locations)



Fatty acids and Metabolic Diseases



Candidate genes

PPARG, G6PC2，APOE, ABCA1, CEPT, LPL, SCD1

Fatty acid profiles

- **Diet**
- **Physical activity**
- **Lifestyle (Smoking, drinking)**

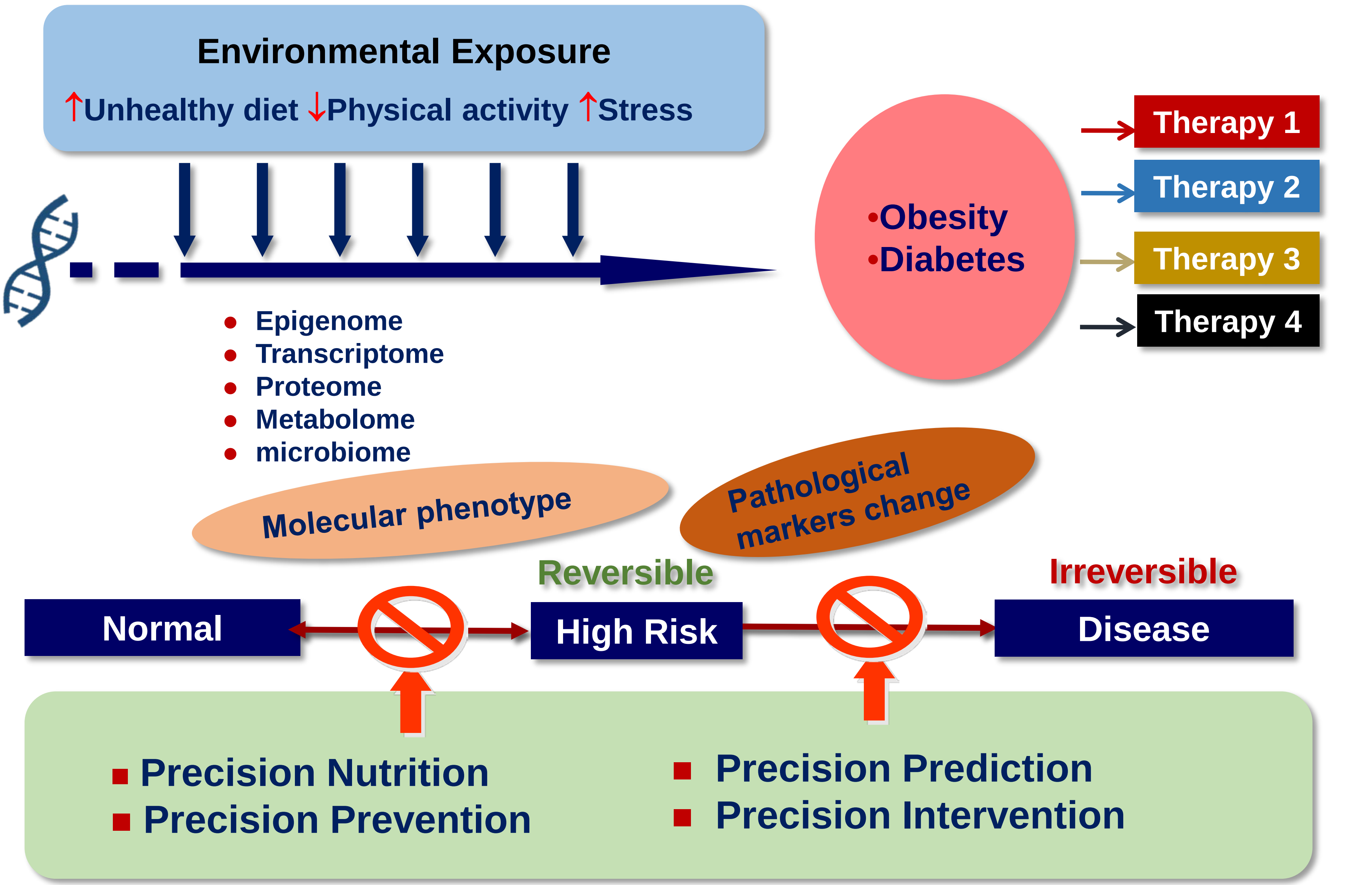
Characteristics of fatty acids and associations with:

- **Obesity (BMI, body fat distribution)**
- **Muscle distribution and function**
- **Cardiovascular (BP, ECG, carotid plaque)**
- **Lung function**
- **Glucose, HbA1c, HDL-c, LDL-c, TC**

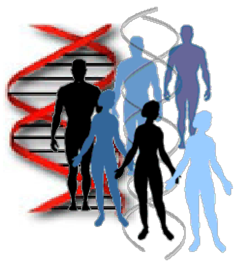
MetS, T2D, Cardiovascular diseases, lung function

- **Identify fatty acids that are closely associated with diseases.**
- **Genetic and environmental factors contributing to fatty acid levels.**
- **Lay foundation for disease prediction.**

National Precision Medicine Project for Metabolic Disease



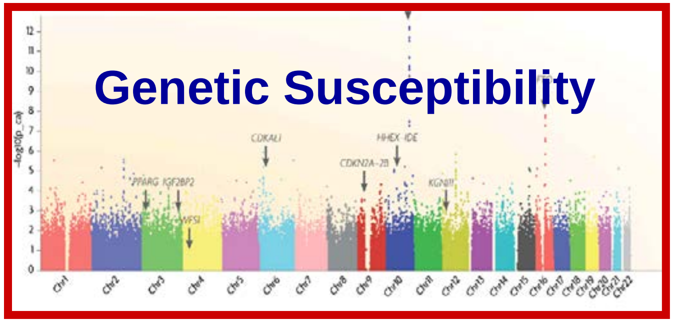
What We Could Do Together?

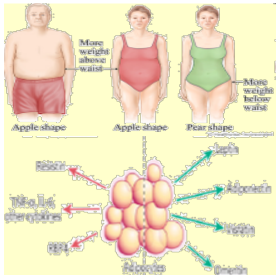


Gene-Gene

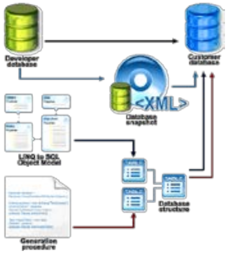
Ethnic Differences

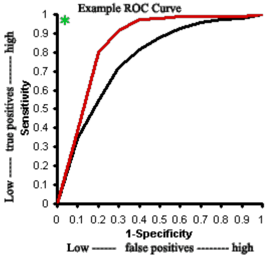
Gene-Environment

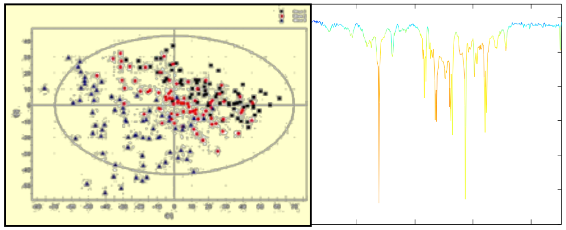




Gene-Phenotype







Matebolomics

Better Nutrition and Better Health

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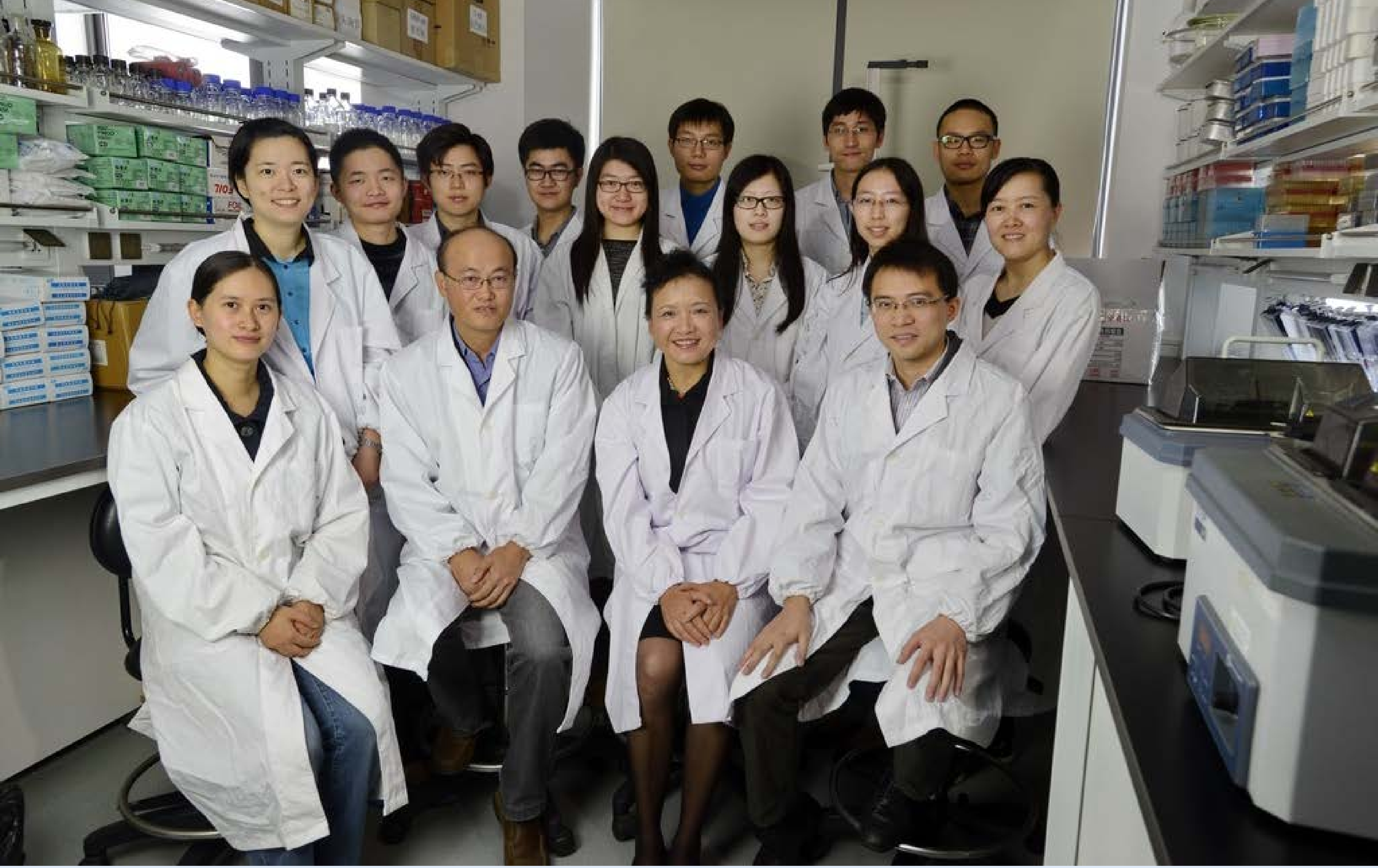
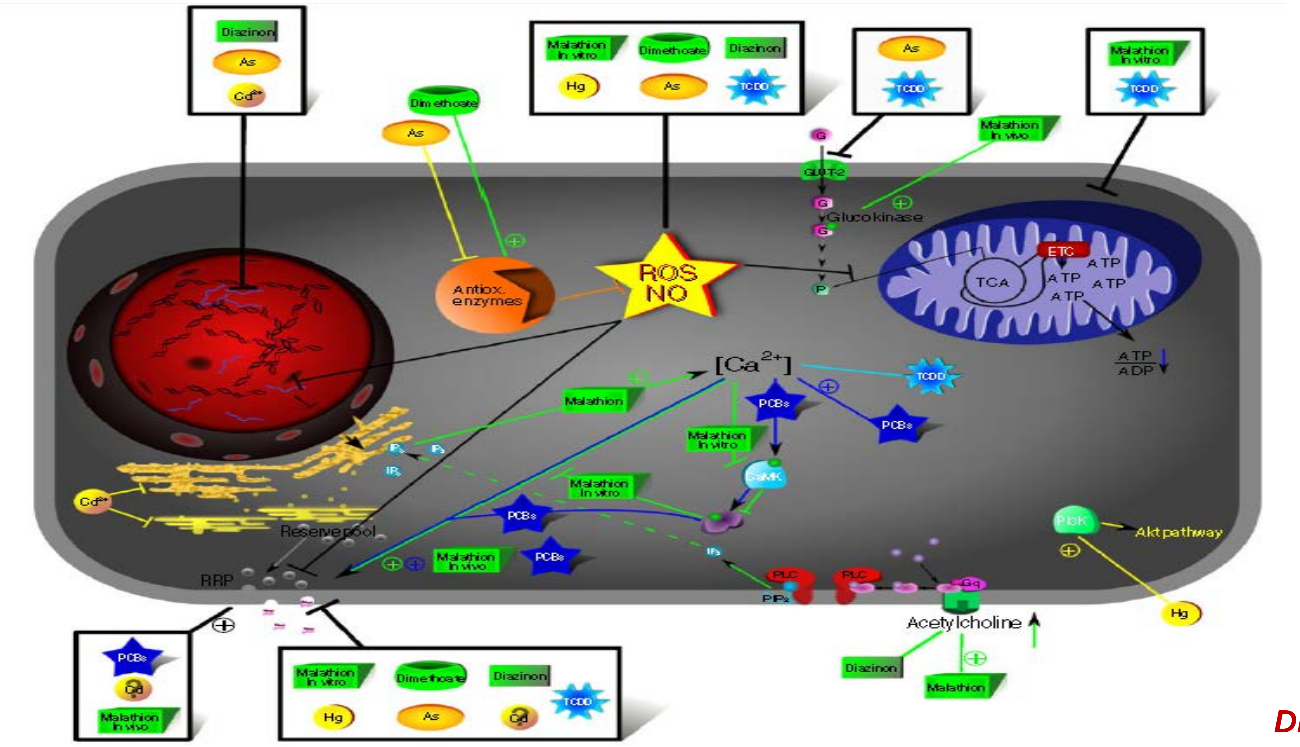


Thanks!

Nickel and Type 2 Diabetes

- Source: alloy, electroplating, nickel-cadmium battery, burning coal, fuel oil and waste.
- Animal studies: induced hyperglycemia.
- Human population-based data : not available



Toxicology (1992)

Diabetologia (2011)

Ecotoxicol Environ Saf (2012)