# *Meta-analyses of Human Genome Studies: Epigenetic Risk Factors and Population Health Issues in the World*

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*School of Nursing, Azusa Pacific University, USA; Department of Nursing, College of Medicine, National Taiwan University, Taiwan*

*2014 July 24-28, Sigma Theta Tau International Research Congress, Hong Kong*

Sigma Theta Tau International
Honor Society of Nursing®

# 25th International Nursing Research Congress
# Faculty Disclosure

| *Faculty Name* | Pamela Shiao, PhD, RN, FAAN |
|---|---|
| *Conflicts of interest:* | None |
| *Employer:* | Azusa Pacific University |
| *Sponsorship / Commercial support* | None |

| *Faculty Name* | Nien-Tzu Chang, PhD, RN |
|---|---|
| *Conflicts of interest:* | None |
| *Employer:* | National Taiwan University |
| *Sponsorship / Commercial support* | None |

| *Faculty Name* | Po-Jui Yu, MSN, DNP Student |
|---|---|
| Conflicts of interest: | None |
| *Employer:* | National Taiwan University |
| *Sponsorship / Commercial support* | None |

| *Faculty Name* | Yen-Chiun Lin, PhD, RN |
|---|---|
| *Conflicts of interest:* | None |
| *Employer:* | National Taiwan University |
| *Sponsorship / Commercial support* | None |

# Purpose

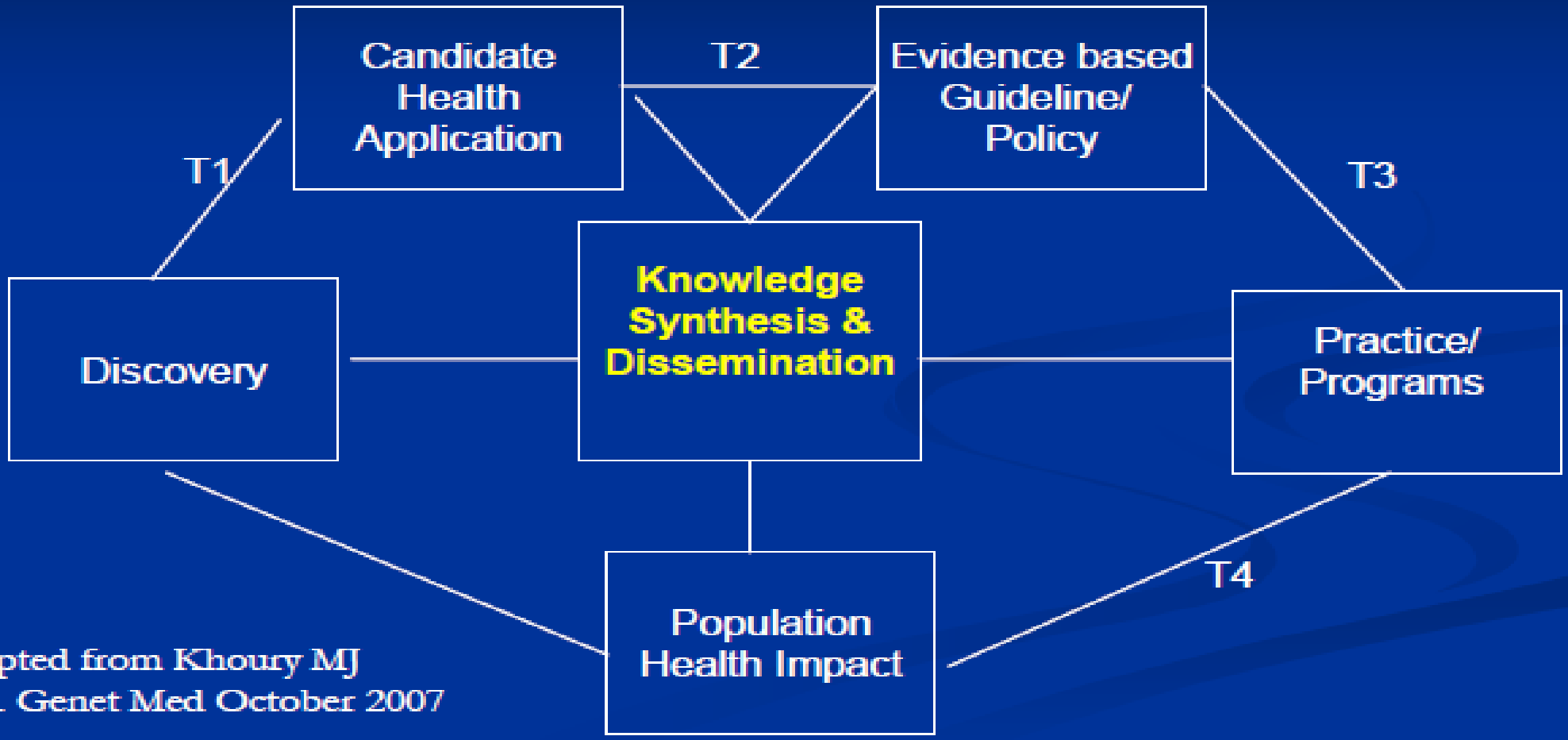
**To disseminate current evidence on:**

**Population Genome Health through the meta-analyses of epigenetic risk factors with the development of Cancers and Cardiovascular Diseases.**

# Learning Objectives

1. **Understand gene mutation variations in relation to chronic diseases for underlying population health issues of various race-ethnicity groups in the world.**
2. **Discuss potential epigenetics and lifestyle prevention strategies to promote cardiovascular health and to prevent cancers and cardiovascular diseases.**

# The Phases of Translation from "Discovery" to "Population Health Impact"




Adapted from Khoury MJ et al. Genet Med October 2007

# *Implementation Science*

**Research-based practice**

**Science-based practice, Evidence-based practice, Research Utilization**

**Levels of Evidence**

- **Clinical projects - Levels 5-7**
- **Research Projects - Levels 2-4**
- **Research Programs**
- **Meta-Analysis - Level 1**

Shiao & Dibble, 2006.

**Table 1.** Hierarchical Classification of Levels of Evidence

| Research Designs | Levels | Descriptions |
|---|---|---|
| Experimental | I | Metaanalysis of randomized control trials |
| | II | Individual randomized control trials |
| | III A | Controlled trials without randomization |
| | III B | Case control trials, within subjects design |
| Association | IV | Systematic reviews of studies with various designs |
| | V | Clinical observation studies — real time, repeated measures, time series designs |
| Descriptive | VI A | Published guidelines from professional organizations |
| | VI B | Descriptive case studies |
| | VII | Quality improvement reports, population-specific trend data |

Data from Attin et al,[18] Levitt et al,[19] Oncology Nursing Society.[20]

# Disrupting Incrementalism in Health Care Innovation

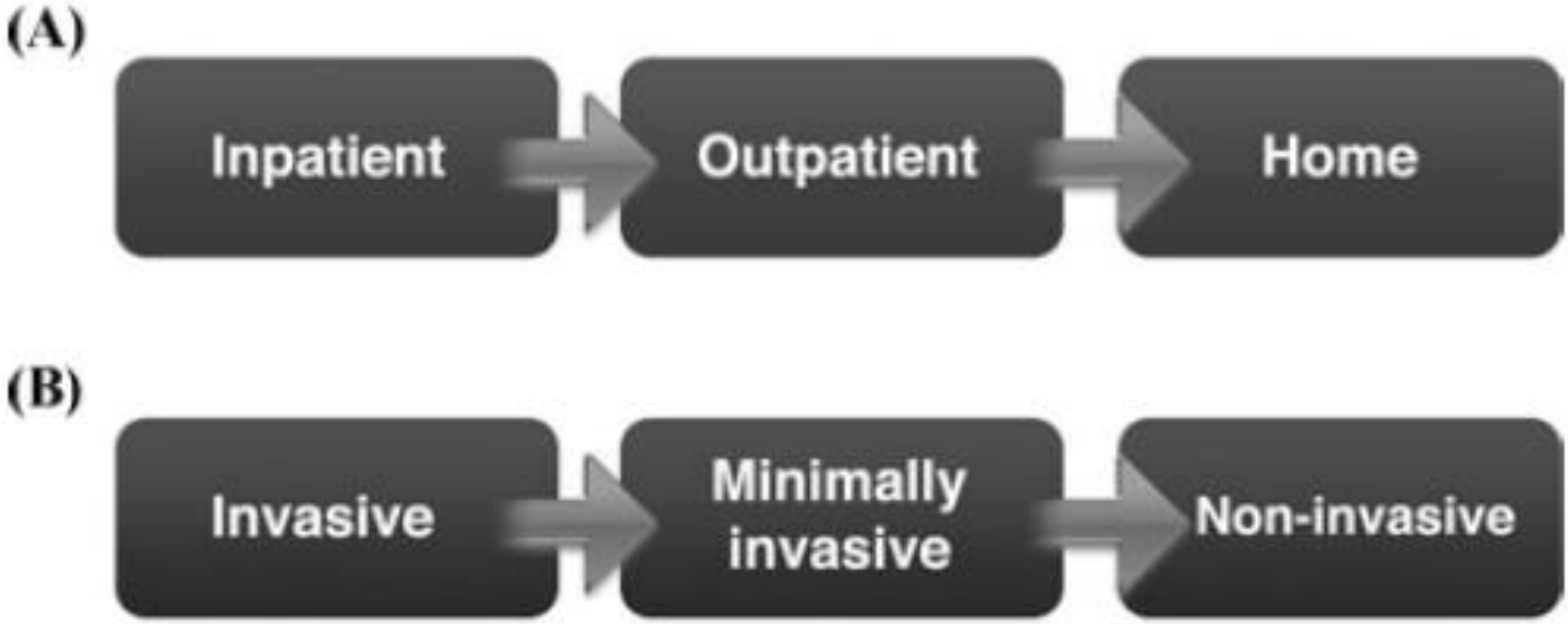



**Figure 1.** Two main mechanisms of disruption in health care innovation: (A) Change of venue disruption model; (B) Degree of invasiveness disruption model.

# $1,000 Genome — Goal set for 2014-2020 by NHGRI


Effective Date: 10 September 2012

"build a device and use it to sequence 100 human genomes within 30 days or less, with an accuracy of no more than one error in every 1,000,000 bases sequenced, with sequences accurately covering at least 98% of the genome, and at a recurring cost of no more than US$1,000 per genome"[1]

baby's

# ABC's of Newborn Screening

Genetic Alliance

Search

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Programs
Registries for All
WGS Stories
Newborn Screening
NSEC(+)

## Programs

Genetic Alliance has developed a series of programs designed to increase the visibility of genetics and advocacy, establish strong networks and advance important campaigns, including community based family history. Our current programs include:

Access to Credible Genetics Resources Network
A Centers for Disease Control and Prevention (CDC) cooperative agreement to provide consumers and health professionals with increased access to quality information on the etiology, diagnosis, treatment and management of individuals with Duchenne and Becker muscular dystrophy (DBMD) and Fragile X syndrome (FXS).

Search

baby's first test

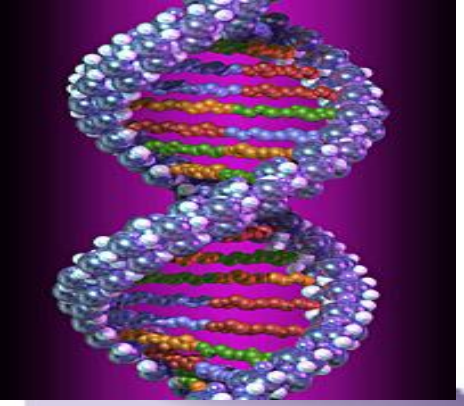
About Newborn Screening | What to Expect | Find A Condition | Living With Conditions | Health Professio

- Screening Facts
- Genetics & Family History
- Screening Resources
- Conditions Screened by State
- Glossary

Newborn Screeni

Newborn screening detec
conditions in 1 in 300 bab

NEXT: NEWBORN SCREENING THE FACTS

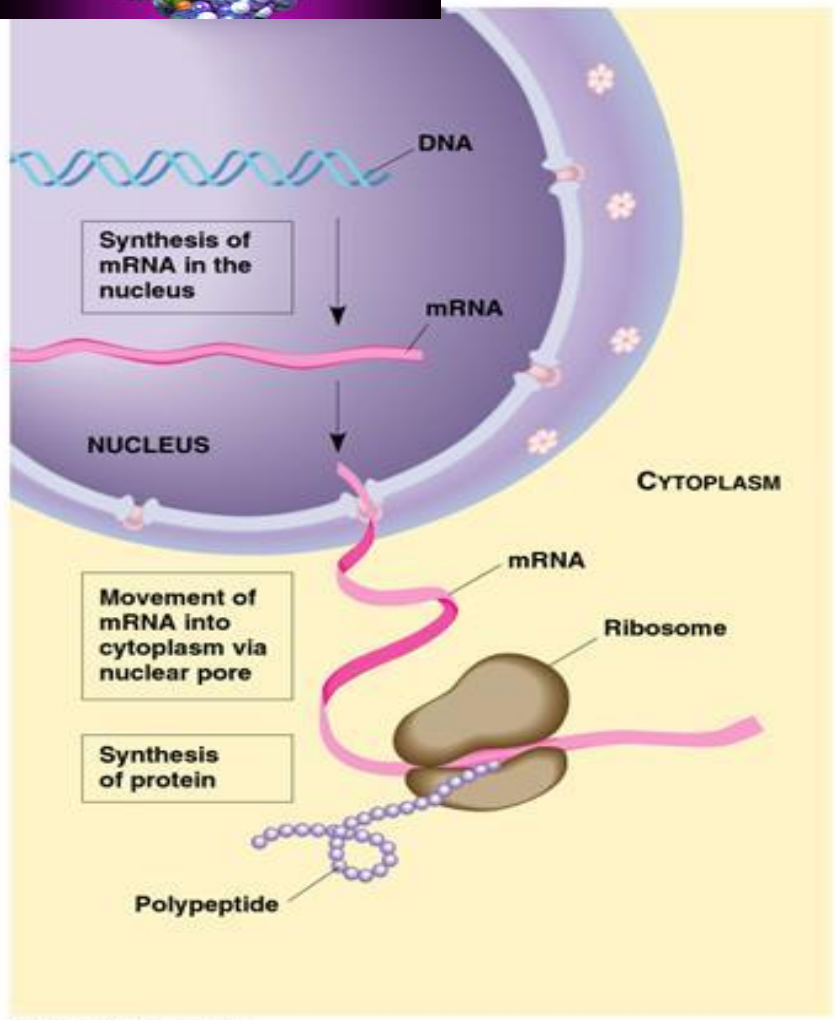


ARTICLE

doi:10.1038/nature10354

# Human metabolic individuality in biomedical and pharmaceutical research

ıin[4]*, Ann-Kristin Petersen[5]*, Robert P. Mohney[6], David Meredith[7], Brigitte Wägele[1,8], RAM†, Panos Deloukas[4], Jeanette Erdmann[9], Elin Grundberg[4,10], Christopher J. Hammond[10], ıbi Kastenmüller[1], Anna Köttgen[13], Florian Kronenberg[14], Massimo Mangino[10], Christa Meisinger[15], Verner Mewes[1,8], Michael V. Milburn[6], Cornelia Prehn[11], Johannes Raffler[1,2], Janina S. Ried[5], h J. Samani[18], Kerrin S. Small[10], H.-Erich Wichmann[19,20,21], Guangju Zhai[10], Thomas Illig[22], ki[11,12], Nicole Soranzo[4]* & Christian Gieger[5]*






FORTUNE

STARTUP STARS

## METABOLON

| | |
|---|---|
| REVENUE | $20 million |
| HEADQUARTERS | Research Triangle Park, N.C. |
| INDUSTRY | Health care |
| FOUNDED | 2000 |
| EMPLOYEES | 100 |

**ODDLY, A DRUG** that helps one cancer victim may not work on another—but doctors don't always have the tools to predict which patients will benefit. Metabolon aims to change that. The company works in an emerging field called personalized medicine where treatments are designed to fit an individual's physical makeup. It can test the small molecules in samples of

## Current approach

- Efficacy = .80
- Reach = .10
- .80 x .10
- Effectiveness = .08

## Public Health model

- Efficacy = .20
- Reach = .50
- .20 x .50
- Effectiveness = .10

# Multiplex Prototype Test

## 8 health conditions & 15 genes

- **Diabetes**
  - ☑ KCNJ11
  - ☑ CAPN10
  - ☑ PPARg
  - ☑ TCF7L2
- **Heart Disease**
  - ☑ APOB
  - ☑ NOS3
  - ☑ CETP
- **High Cholesterol**
  - ☑ LIPC
- **Hypertension**
  - ☑ AGT
- **Lung cancer**
  - ☑ MPO
- **Colon Cancer**
  - ☑ MTHFR
- **Skin Cancer**
  - ☑ MC1R
- **Osteoporosis**
  - ☑ ESR1
  - ☑ IL6
  - ☑ COL1A1


Original Paper

Public Health Genomics

Considerations for Designing a Prototype Genetic Test for Use in Translational Research

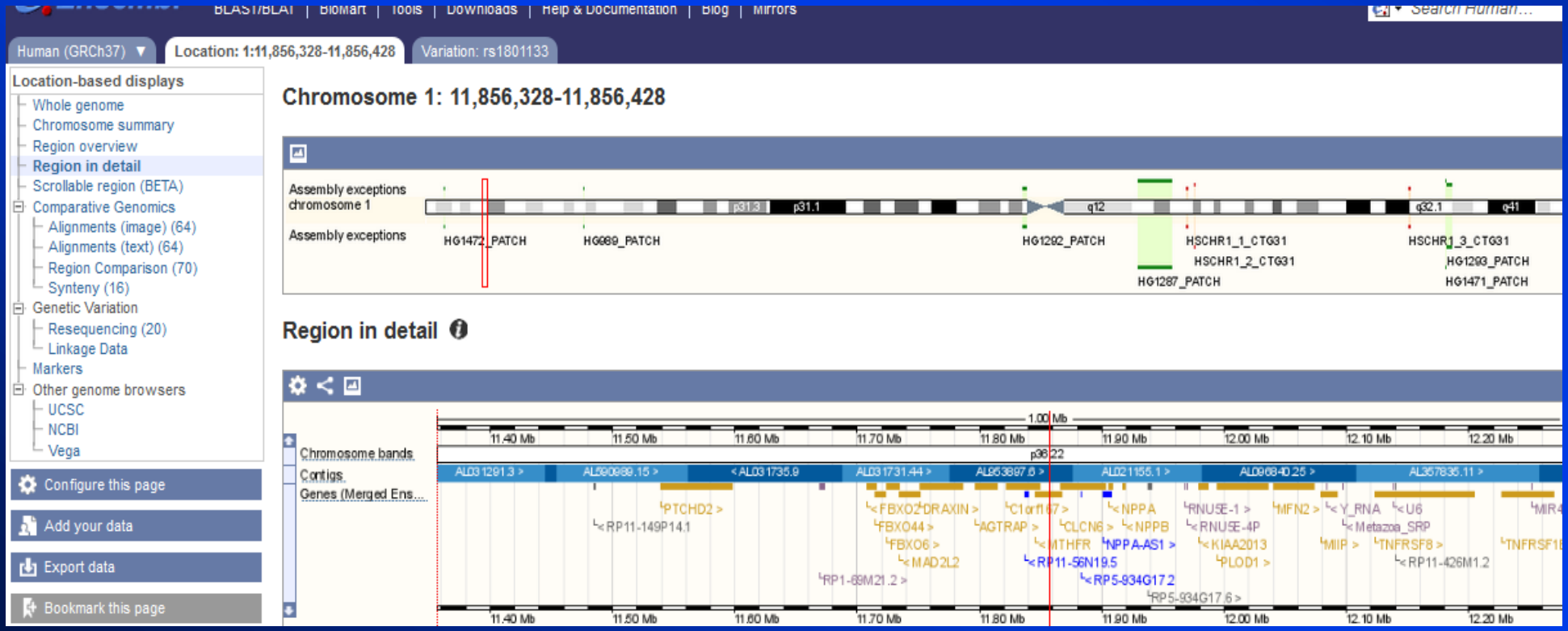
C.M. McBride

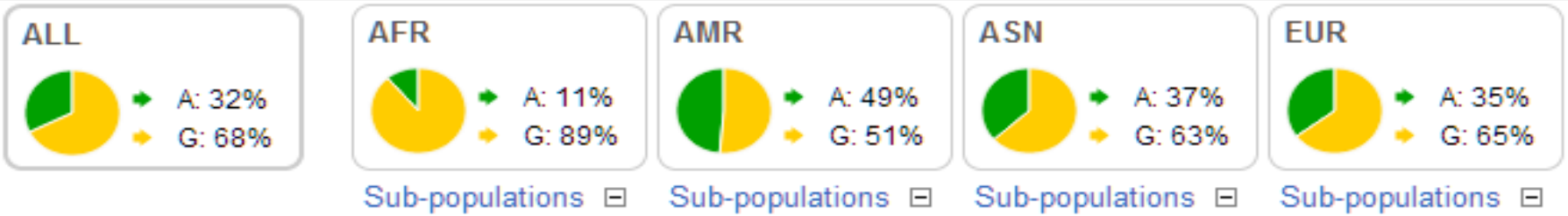
Colleen M. McBride, Ph.D.
Social and Behavioral Research Branch
April 18, 2012

# *Ensembl*

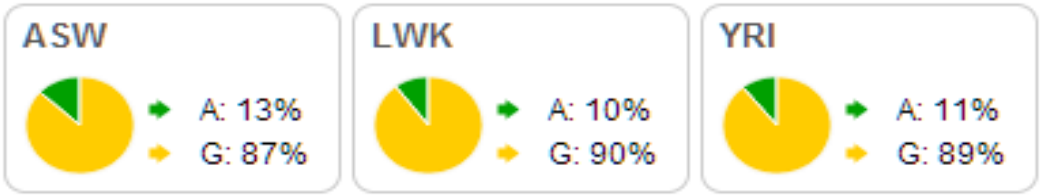
**http://uswest.ensembl.org/index.html**

- **Genome browser**
- **Search by gene or variation (rs number)**
  - **rs # = reference SNP**

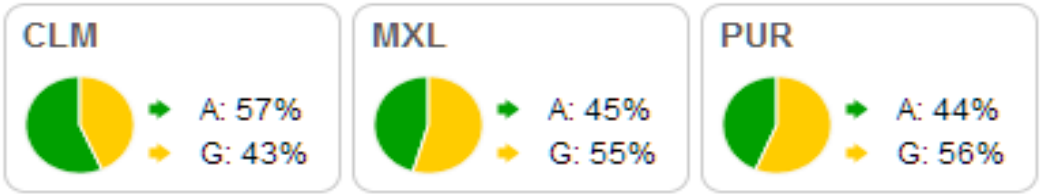




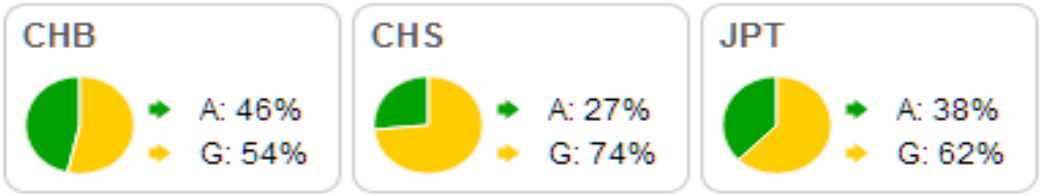

AFR sub-populations



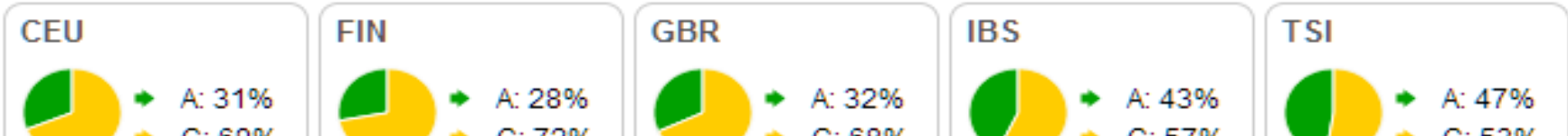

AMR sub-populations




Colombian from Medellin, Colombia




EUR sub-populations








Sub-populations ⊟ Sub-populations ⊟ Sub-populations ⊟ Sub-populations ⊟

## AFR sub-populations

### ASW


### LWK


### YRI


## AMR sub-populations

### CLM


### MXL


### PUR


## ASN sub-populations

### CHB


### CHS


### JPT


## EUR sub-populations

British in England and Scotland

### CEU


### FIN


### GBR


### IBS

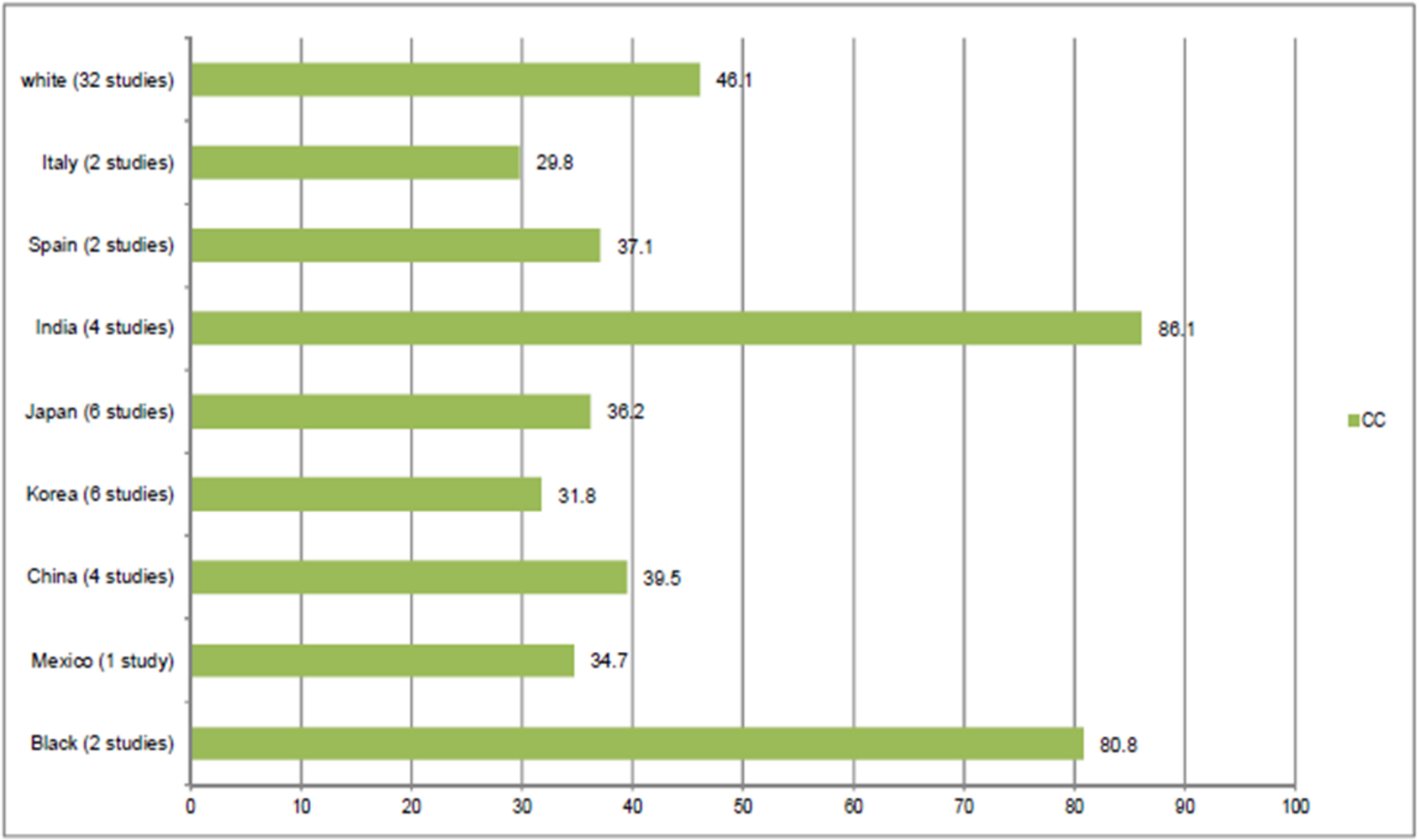

### TSI

Ancestry Composition tells you what percent of your DNA comes from each of 31 populations worldwide. The analysis includes DNA you received from all of your ancestors, on both sides of your family. The results reflect where your ancestors lived 500 years ago, before ocean-crossing ships and airplanes came on the scene.

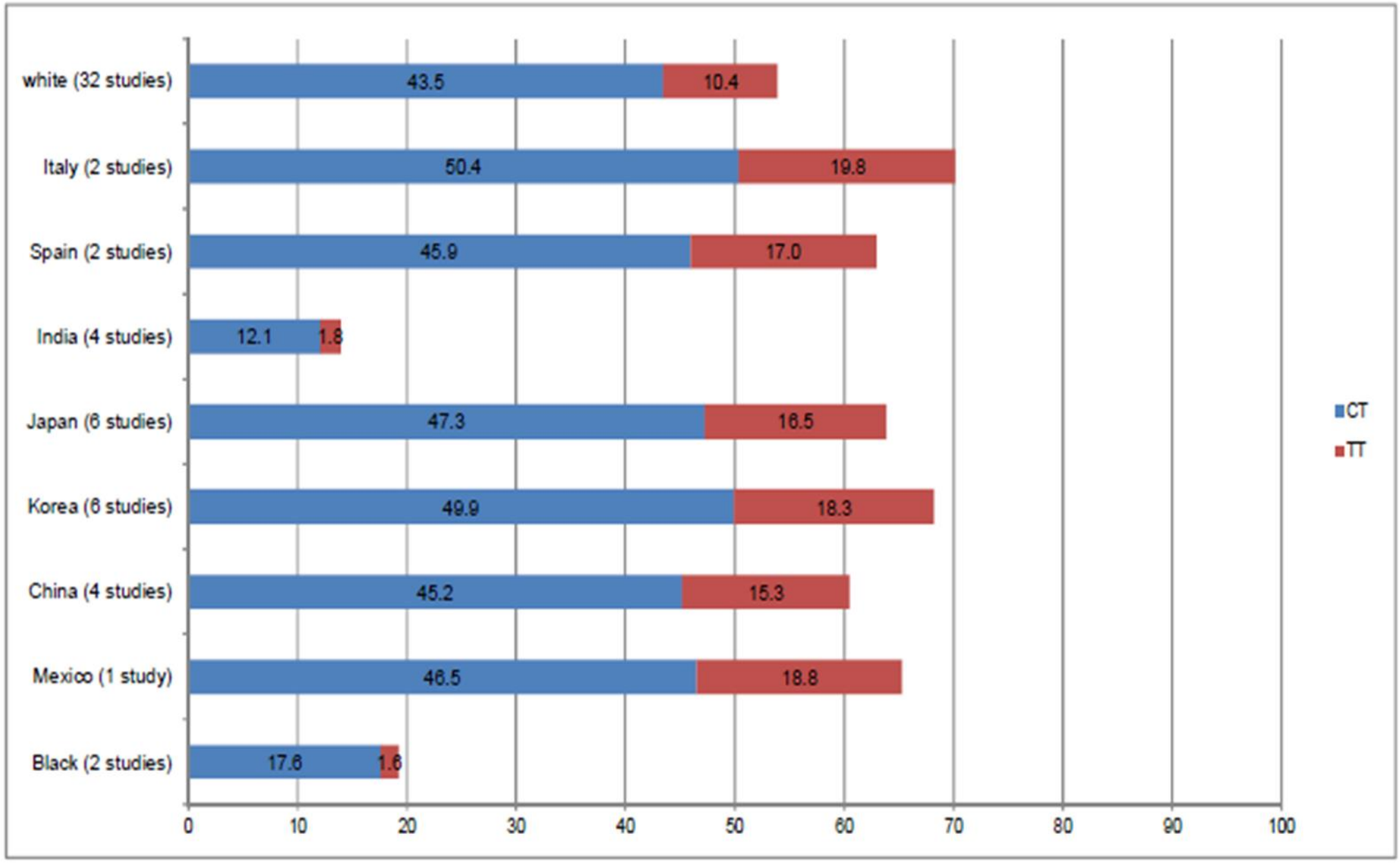
- **99.6%** East Asian & Native American
  - 99.6% East Asian
  - ? Southeast Asian
  - 0.0% Native American
  - 0.0% Nonspecific East Asian & Native Am...
- **0.3%** European
  - 0.0% Northern European
  - 0.0% Southern European
  - 0.0% Eastern European
  - 0.0% Ashkenazi
  - 0.3% Nonspecific European
- **0.0%** Middle Eastern & North African
  - 0.0% Middle Eastern
  - 0.0% North African

MTHFR 677

CC

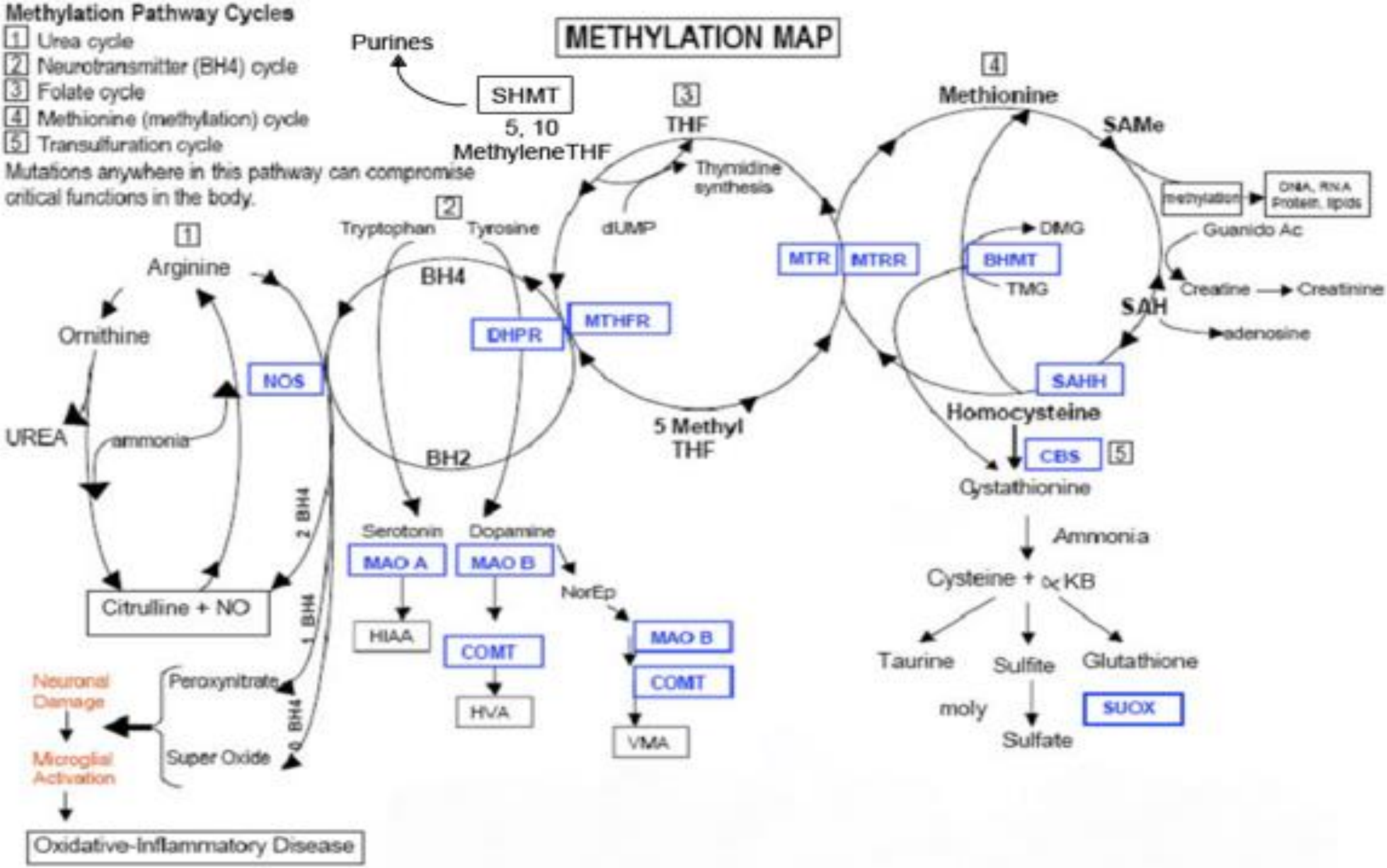

white (32 studies)
46.1
Italy (2 studies)
29.8
Spain (2 studies)
37.1
India (4 studies)
86.1
Japan (6 studies)
36.2
Korea (6 studies)
31.8
China (4 studies)
39.5
Mexico (1 study)
34.7
Black (2 studies)
80.8
0
10
20
30
40
50
60
70
80
90
100
CC

CT+TT


white (32 studies)
43.5
10.4
Italy (2 studies)
50.4
19.8
Spain (2 studies)
45.9
17.0
India (4 studies)
12.1
1.8
Japan (6 studies)
47.3
16.5
Korea (6 studies)
49.9
18.3
China (4 studies)
45.2
15.3
Mexico (1 study)
46.5
18.8
Black (2 studies)
17.6
1.6
0
10
20
30
40
50
60
70
80
90
100
CT
TT

| | | | | |
|---|---|---|---|---|
| 27 | RPS3AP46 | chr14:54,069,442-54,090,123 | 20,682 | pseudogene |
| 28 | RHPN2 | chr19:33,469,498-33,555,824 | 86,327 | |
| 29 | CDH1 | chr16:68,771,195-68,869,444 | 98,250 | |
| 30 | KRT8P16 | chr10:8,568,699-8,594,564 | 25,866 | pseudogene |
| 31 | TCEB1P3 | chr10:10,206,117-10,226,740 | 20,624 | pseudogene |
| 32 | MTHFR | chr1:11,845,787-11,866,160 | 20,374 | |
| 33 | MTR | chr1:236,958,581-237,067,281 | 108,701 | |
| 34 | MTRR | chr5:7,869,217-7,901,235 | 32,019 | |
| 35 | MTHFD1 | chr14:64,854,759-64,926,725 | 71,967 | |
| 36 | UGT1A1 | chr2:234,668,919-234,681,951 | 13,033 | |
| 37 | MLH1 | chr3:37,034,841-37,092,337 | 57,497 | |
| 38 | MSH2 | chr2:47,630,263-47,710,360 | 80,098 | |
| 39 | MSH6 | chr2:48,010,221-48,034,092 | 23,872 | |
| 40 | PMS2 | chr7:6,012,870-6,048,737 | 35,868 | |
| 41 | TP53 | chr17:7,571,720-7,590,863 | 19,144 | |
| 42 | Kras | chr12:25,358,180-25,403,854 | 45,675 | |
| 43 | | total size | 2,107,283 | |

| Test | MTHFR C677T | MTHF A1298C | MTHFD1 G1958A | MTR A2756G | MTRR A66G |
|---|---|---|---|---|---|
| buccal swab 2 Hispanic | CT | AA | GA | AA | AA |
| buccal swab 3* EA | CC | AC | GA | AA | AA |
| buccal swab 5 Asian | CC | AC | GG | AA | AG |
| buccal swab 6 EA | TT | AA | GG | AA | GG |
| buccal swab 7 Asian | CT | AC | GG | AA | AG |
| buccal swab 8 Asian | CC | CC | GG | AA | AG |
| buccal swab 9 Asian | CT | AA | GG | AA | AA |
| buccal swab 10 EA | CC | AC | GG | AG | AA |
| buccal swab 11 Asian | CT | AA | GG | AA | AA |
| buccal swab 12 Asian | CT | AC | AA | AA | AA |
| Wild type | 4 CC | 4 AA | 7 GG | 9 AA | 6 AA |
| Heterozygous | 5 CT | 5 AC | 2 GA | 1 AG | 3 AG |
| Homozygous | 1 TT | 1 CC | 1 AA | 0 GG | 1 GG |

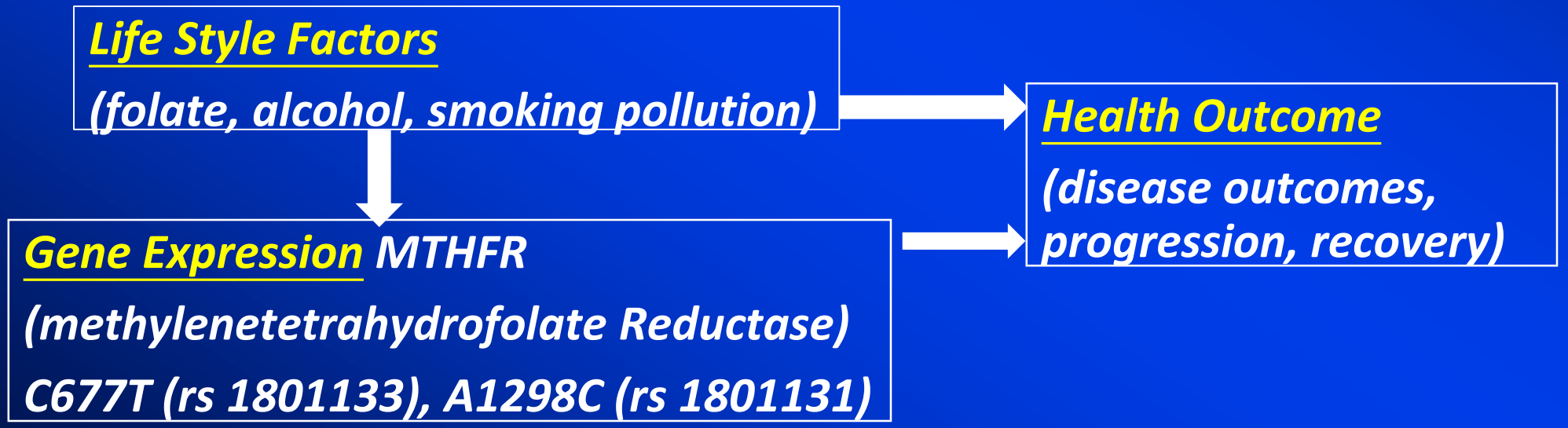

Methylation Pathway Cycles
1 Urea cycle
2 Neurotransmitter (BH4) cycle
3 Folate cycle
4 Methionine (methylation) cycle
5 Transulfuration cycle
Mutations anywhere in this pathway can compromise critical functions in the body.
METHYLATION MAP
Purines
SHMT
5, 10 MethyleneTHF
3
THF
Thymidine synthesis
dUMP
4
Methionine
SAMe
methylation
DNA, RNA Protein, lipids
Guanido Ac
Creatine
Creatinine
DMG
TMG
BHMT
MTR
MTRR
SAH
adenosine
SAHH
Homocysteine
CBS
5
Cystathionine
Ammonia
Cysteine + αKB
Taurine
Sulfite
Glutathione
moly
SUOX
Sulfate
1
Arginine
Ornithine
UREA
ammonia
NOS
Citrulline + NO
2 BH4
1 BH4
Q BH4
Peroxynitrate
Super Oxide
Neuronal Damage
Microglial Activation
Oxidative-Inflammatory Disease
2
Tryptophan
Tyrosine
BH4
BH2
DHPR
MTHFR
5 Methyl THF
Serotonin
Dopamine
MAO A
MAO B
NorEp
HIAA
COMT
HVA
MAO B
COMT
VMA

# Epigenetic Factors

*Epigenetics The study of heritable changes in gene activity which are not caused by changes in the DNA sequence*

*- Gene expression or cellular phenotype*

*- DNA methylation and histone modification, repressor proteins that attach to silencer*



# Lifestyles and CR Cancer (CRC)

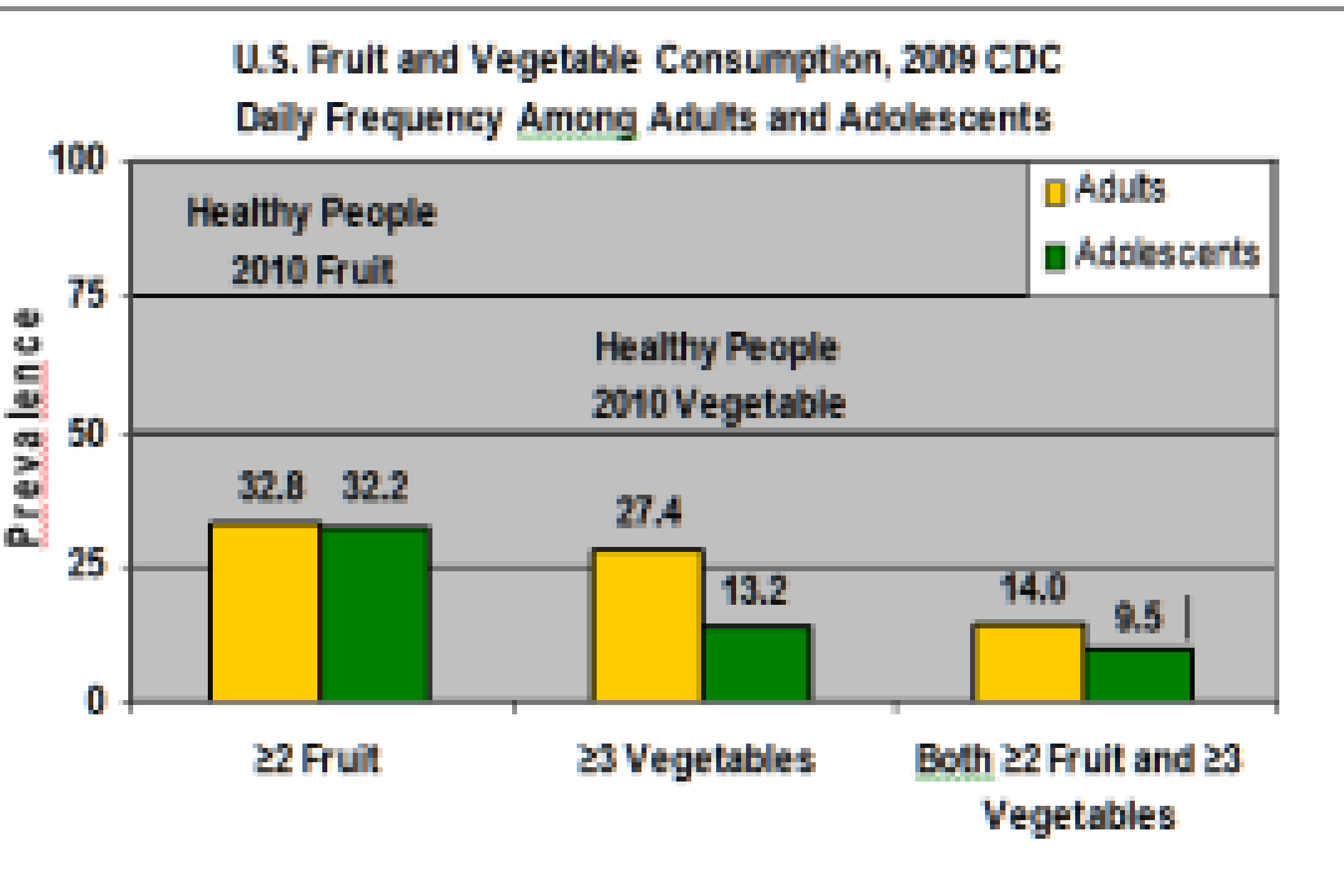
| (# of studies) | CRC n (%) | *Control n (%)* | RR (95% CI) | p-value |
|---|---|---|---|---|
| Low Folate (20) < 116-343 mcg/day | 3,995 (33.6) | 5,167 (30.42) | 1.1125 | < 0.01 |
| Low B6 (6) < 1.46-2.55 mg/day | 1,273 (43.97) | 1,802 (39.71) | 1.1391 | < 0.001 |
| Alcohol (19) > 1.44- 30 g/day | 2,907 (41.04) | 3,961 (41.26) | 1.1932 | < 0.01 |
| No smoking (19) | 6,178 (67.88) | 7,839 (69.44) | 0.943 | < 0.05 |

Primary prevention of coronary heart disease: integration of new data, evolving views, revised goals, and role of rosuvastatin in management. A comprehensive survey.Richard Kones. Drug Des Devel Ther 2011; 5: 325–380. Published online 2011 June 13. doi: 10.2147/DDDT.S14934. PMCID: PMC3140289

**Table 3** Cardiovascular risk factors as reported in the 2011 Heart and Stroke Foundation Report[38]

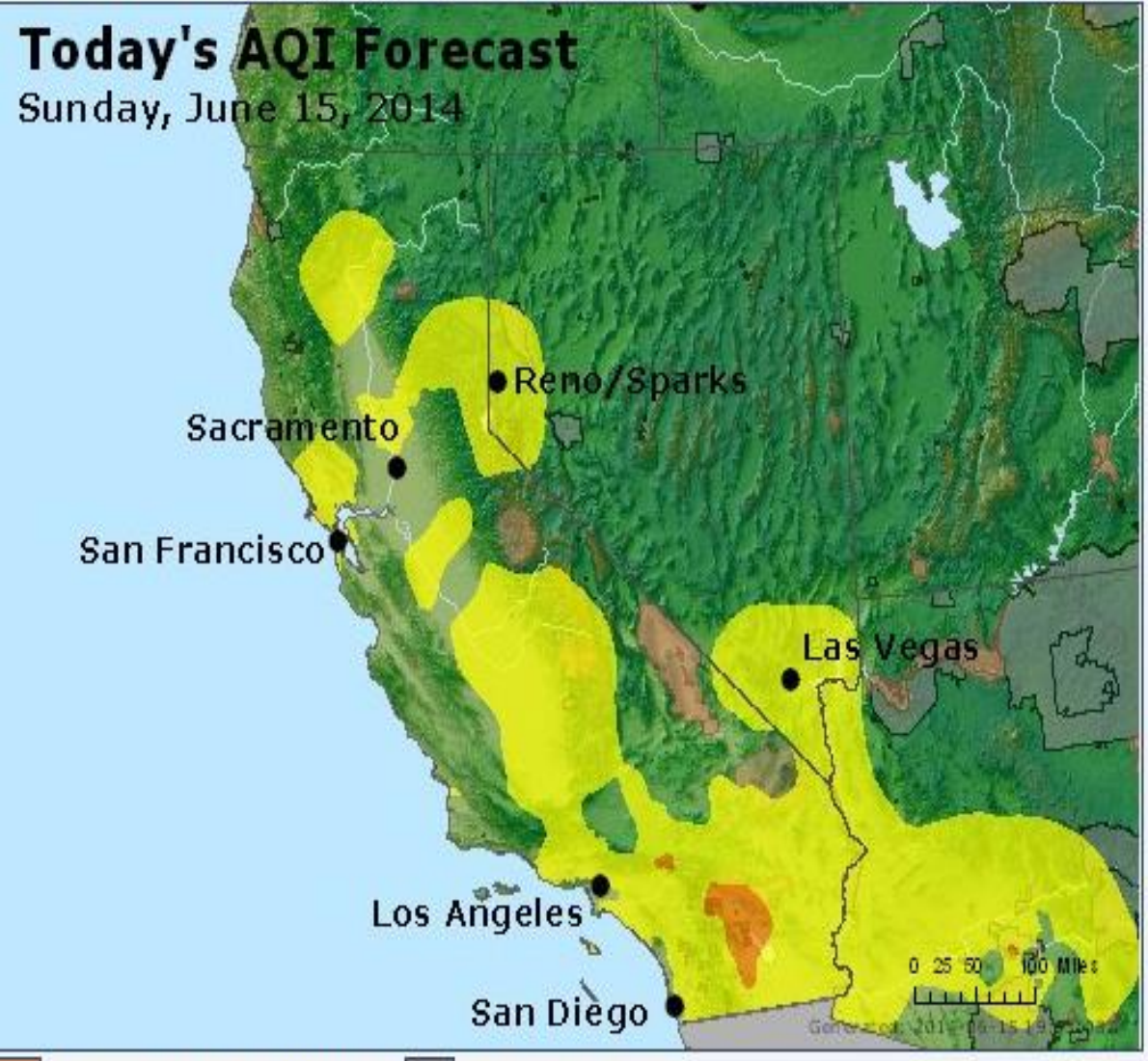
| Risk factor | Self-reported perception (% participation) | Actual prevalence (%, estimated) | Not assessed by health care provider (%) | Impact upon life expectancy (years) |
|---|---|---|---|---|
| Smoking | 23 | 20 | 37 | −13.9 |
| Obesity (age 18 or over) | 18 | 24 | Weight: 40%<br>Waist measure: 67% | −4.0 |
| Physically inactive in leisure time | 31 | 48 | 44 | −3.6 |
| High blood pressure | 17 | 19 | 18 | −2.4 |
| Vegetable and fruit intake <5+/day | 39 | 54 | 52 | −1.3 |

Data from the Heart and Stroke Foundation (HSF) poll of 2000 Canadians performed in December 2010, self-reported from the 2009 Canadian Community Health Survey.


U.S. Fruit and Vegetable Consumption, 2009 CDC
Daily Frequency Among Adults and Adolescents
Prevalence
100
75
50
25
0
Healthy People
2010 Fruit
Healthy People
2010 Vegetable
Adults
Adolescents
32.8
32.2
27.4
13.2
14.0
9.5
≥2 Fruit
≥3 Vegetables
Both ≥2 Fruit and ≥3
Vegetables

| AQI | Air Pollution Level | Health Implications |
|---|---|---|
| 0 - 50 | Good | Air quality is considered satisfactory, and air pollution poses little or no risk |
| 51 -100 | Moderate | Air quality is acceptable; however, for some pollutants there may be a moderate health concern for a very small number of people who are unusually sensitive to air pollution. |
| 101-150 | Unhealthy for Sensitive Groups | sensitive groups may experience health effects. The general public is not likely to |
| 151-200 | Unhealthy | Everyone may begin to experience health effects; members of sensitive groups may experience more serious health effects |
| 201-300 | Very Unhealthy | Health warnings of emergency conditions. The entire population is more likely to be affected. |
| 300+ | Hazardous | Health alert: everyone may experience more serious health effects |

To know more about Air Quality and Pollution, check the wikipedia Air Quality topic or the airnow guide to Air Quality a



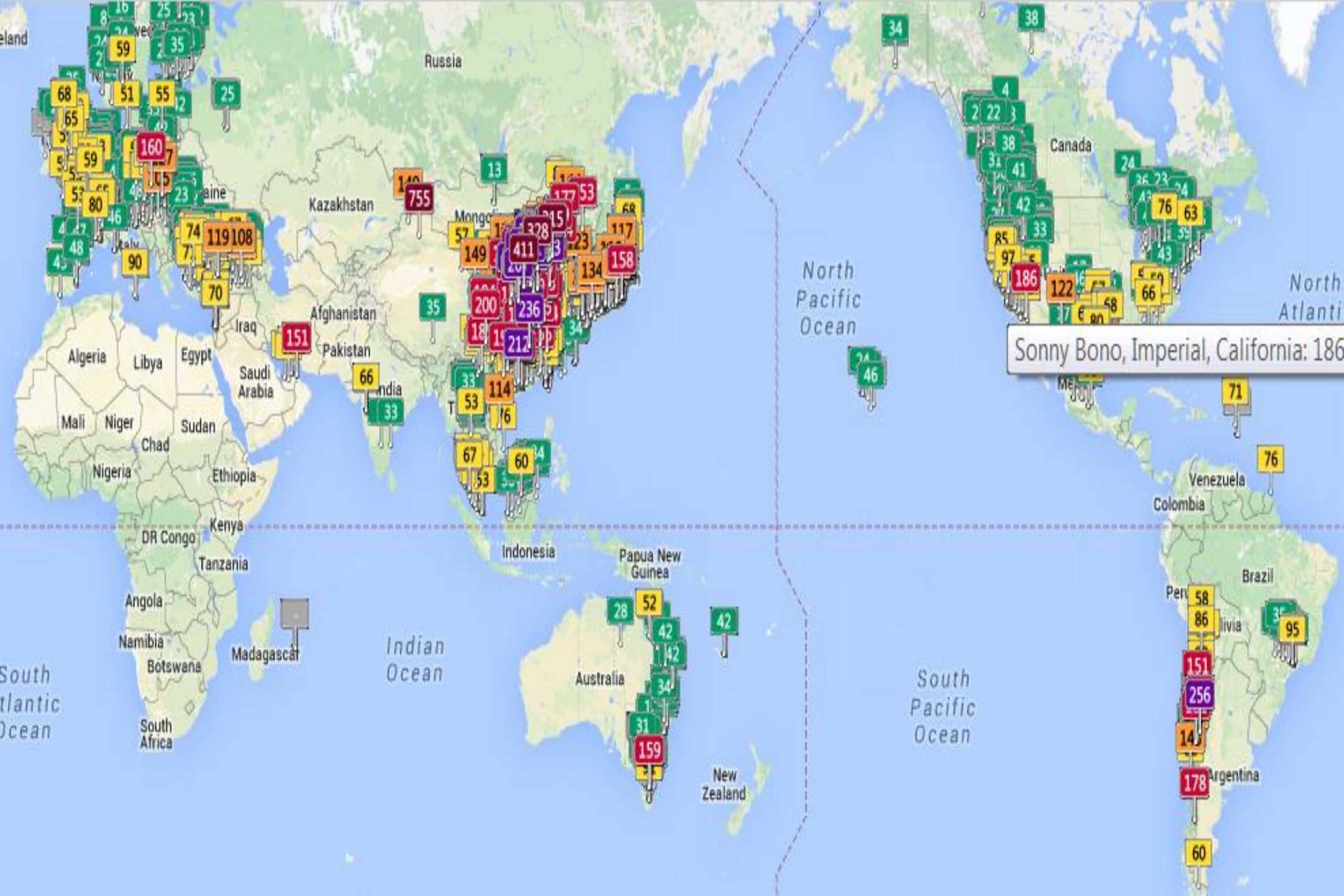

National Parks/Monuments  Tribal Boundaries

The tribal boundaries shown here are provided by the Bureau of Indian Affairs and are intended to be used as a general spatial reference only. They are not a formal determination of tribal boundaries by the EPA.

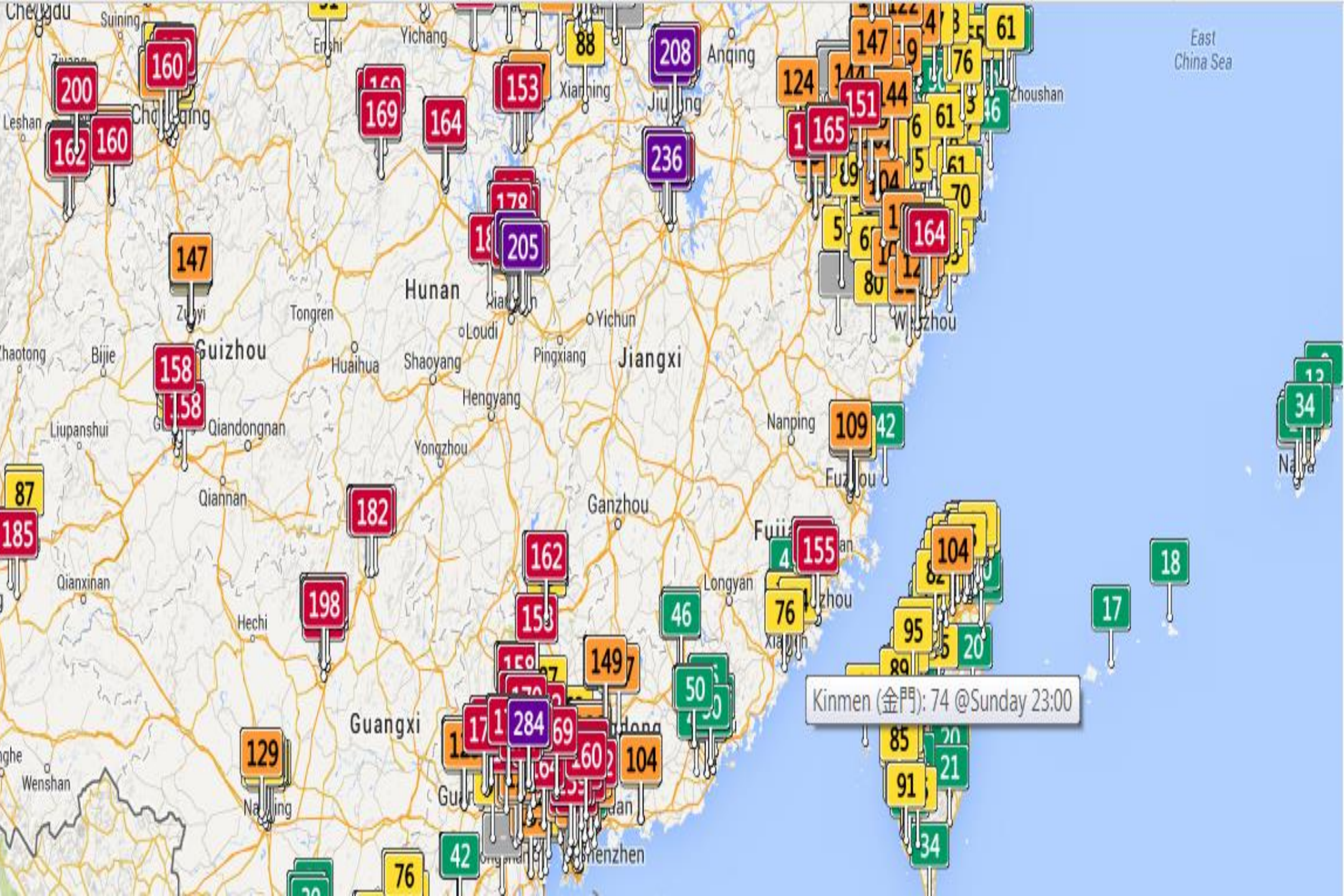
Good | Moderate | USG | Unhealthy | Very Unhealthy | Hazardous | ! Action Day

printable summary

| Reservation | Jun 15 | Jun 16 | |
|---|---|---|---|
| **Los Angeles Area** | | | |
| Antelope Vly | 46 | 51 | 47 |
| Anza Vly | 55 | 53 | 48 |
| Banning | n/a | 111 | 61 |
| Barstow | 47 | 46 | 47 |
| Big Bear Lake | 51 | n/a | n/a |
| C San Bernardino M | n/a | 111 | 54 |
| C San Bernardino-1 | 72 | 72 | 44 |
| C San Bernardino-2 | 72 | 48 | n/a |
| Capistrano Vly | n/a | 55 | 36 |
| Central Coastal | 55 | n/a | 48 |


Sonny Bono, Imperial, California: 186
Russia
Kazakhstan
Canada
Afghanistan
Pakistan
Iraq
Algeria
Libya
Egypt
Saudi Arabia
Mali
Niger
Sudan
Chad
Nigeria
Ethiopia
Kenya
DR Congo
Tanzania
Angola
Namibia
Botswana
South Africa
Madagascar
Indonesia
Papua New Guinea
Australia
New Zealand
Venezuela
Colombia
Brazil
Peru
Bolivia
Argentina
North Pacific Ocean
South Pacific Ocean
Indian Ocean
South Atlantic Ocean
North Atlanti


Wulumuqi (乌鲁木齐): 755 @Monday 3:00
Mongolia
China
North Korea
Sea of Japan
East China Sea
Sapporo
Tokyo
Hong Kong
Macau
Hanoi
Laos
Myanmar (Burma)
Bangladesh
Bhutan
Kolkata
Yangon
Luzon


Kinmen (金門): 74 @Sunday 23:00
East China Sea
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Guizhou
Jiangxi
Guangxi
Yichang
Anqing
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Jiujiang
Zhoushan
Leshan
Suining
Enshi
Zunyi
Tongren
Bijie
Huaihua
Shaoyang
Loudi
Yichun
Pingxiang
Hengyang
Liupanshui
Qiandongnan
Yongzhou
Nanping
Fuzhou
Qiannan
Ganzhou
Qianxinan
Hechi
Longyan
Wenshan
Nanning
Shenzhen
160
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205
124
151
165
61
76
46
70
164
147
158
158
109
42
87
185
182
162
153
198
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284
69
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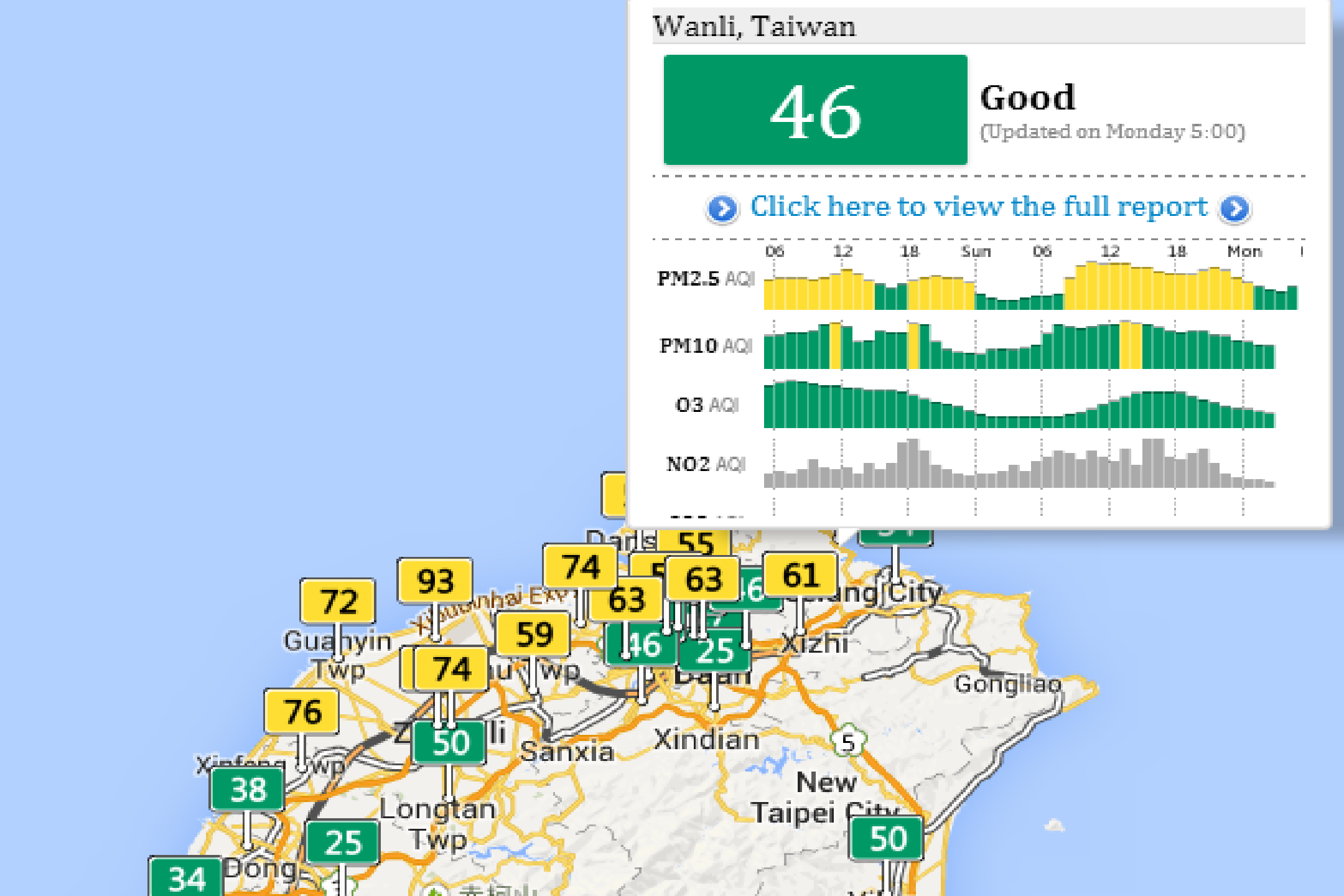
104
129
95
20
85
21
91
34
76
42


Wanli, Taiwan
46
Good
(Updated on Monday 5:00)
Click here to view the full report
06
12
18
Sun
06
12
18
Mon
PM2.5 AQI
PM10 AQI
O3 AQI
NO2 AQI
72
93
74
63
61
59
46
25
76
50
38
25
34
50
Guanyin Twp
Sanxia
Xindian
Xizhi
Gongliao
Longtan Twp
New Taipei City
5

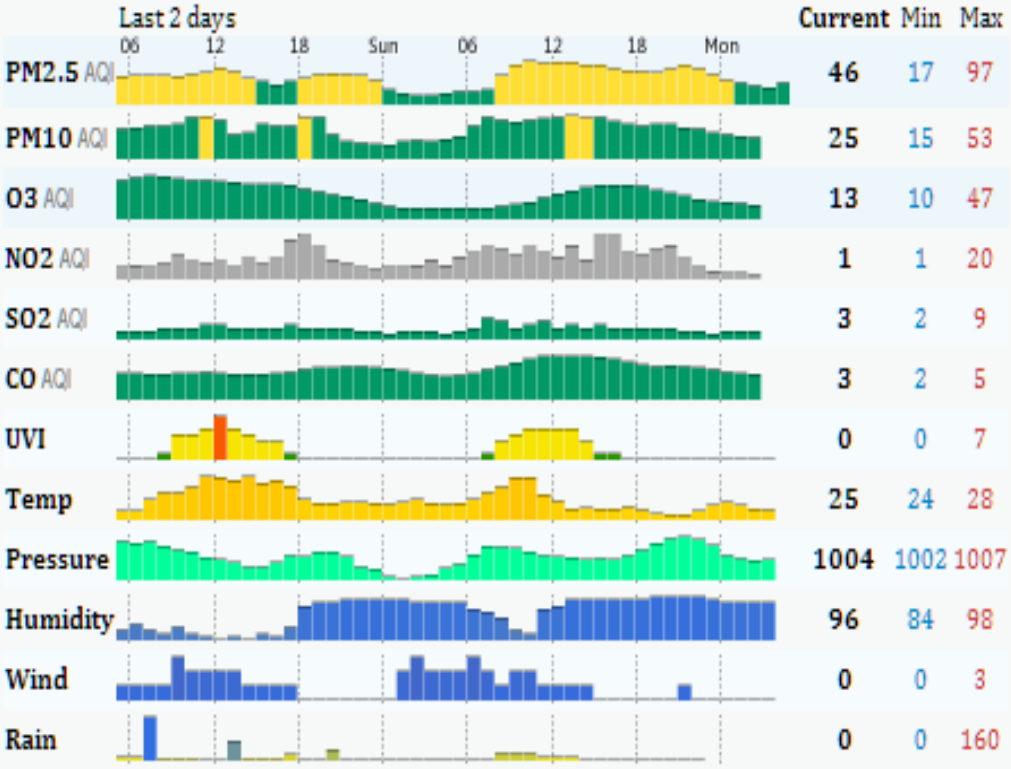
## Wanli AQI: Wanli Real-time Air Quality Index (AQI).

**46**

# Good

Updated on Monday 5:00

Temp: 25°C



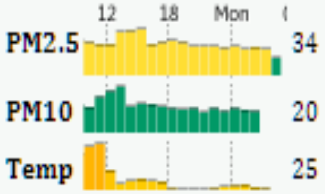

| | Current | Min | Max |
|---|---|---|---|
| PM2.5 AQI | 46 | 17 | 97 |
| PM10 AQI | 25 | 15 | 53 |
| O3 AQI | 13 | 10 | 47 |
| NO2 AQI | 1 | 1 | 20 |
| SO2 AQI | 3 | 2 | 9 |
| CO AQI | 3 | 2 | 5 |
| UVI | 0 | 0 | 7 |
| Temp | 25 | 24 | 28 |
| Pressure | 1004 | 1002 | 1007 |
| Humidity | 96 | 84 | 98 |
| Wind | 0 | 0 | 3 |
| Rain | 0 | 0 | 160 |

## Keelung Air Quality.

**34**

**Good**

Updated on Monday 5:00

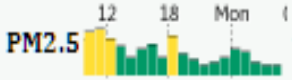



## Yangming Air Quality.

**25**

**Good**

Updated on Monday 4:00

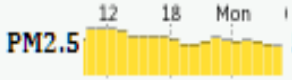



## Shilin Air Quality.

**55**

**Moderate**

Updated on Monday 5:00




## Songshan Air Quality.

**46**

**Good**

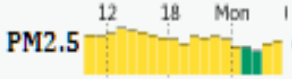
Updated on Monday 5:00


## Zhongshan Air Quality.

**63**

**Moderate**

Updated on Monday 5:00

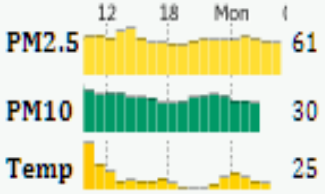



## Xizhi Air Quality.

**61**

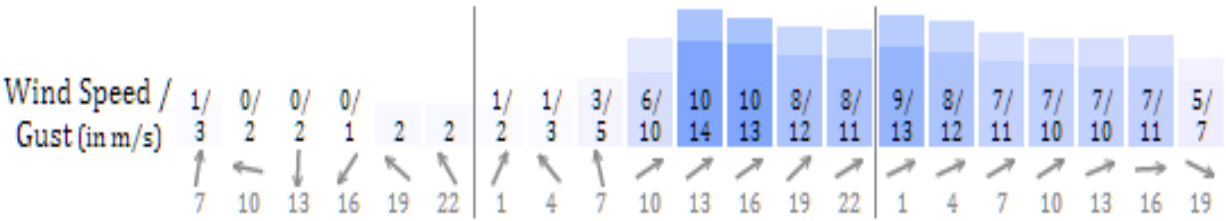
**Moderate**

Updated on Monday 5:00




## Wanli Wind Forecast

*Strong winds can help to lower the pollution*



IPCS Home
Health impacts of chemicals
Tools for assessing chemical risks
Poisons information, prevention and management
Chemical incidents and emergencies
Capacity building

# Toxicogenomics

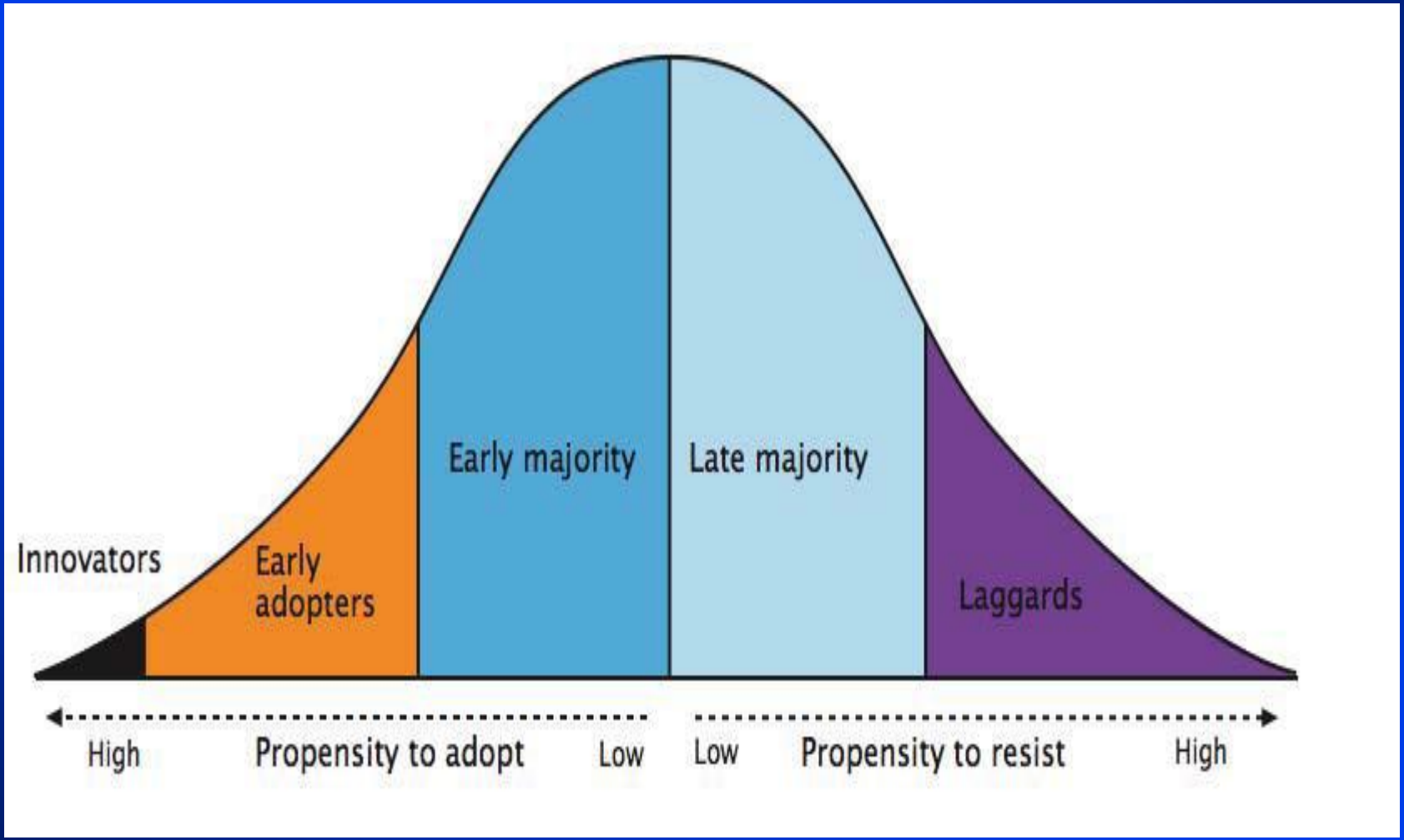
Share

The use of the evolving science of toxicogenomics and its accompanying tools are of great interest to risk assessors, and are being considered as potential ways to improve toxicology and risk methodologies, helping to elucidate the mechanism and mode of action of chemicals among other things.

Twin workshops were organized in 2003-2004 focusing on:

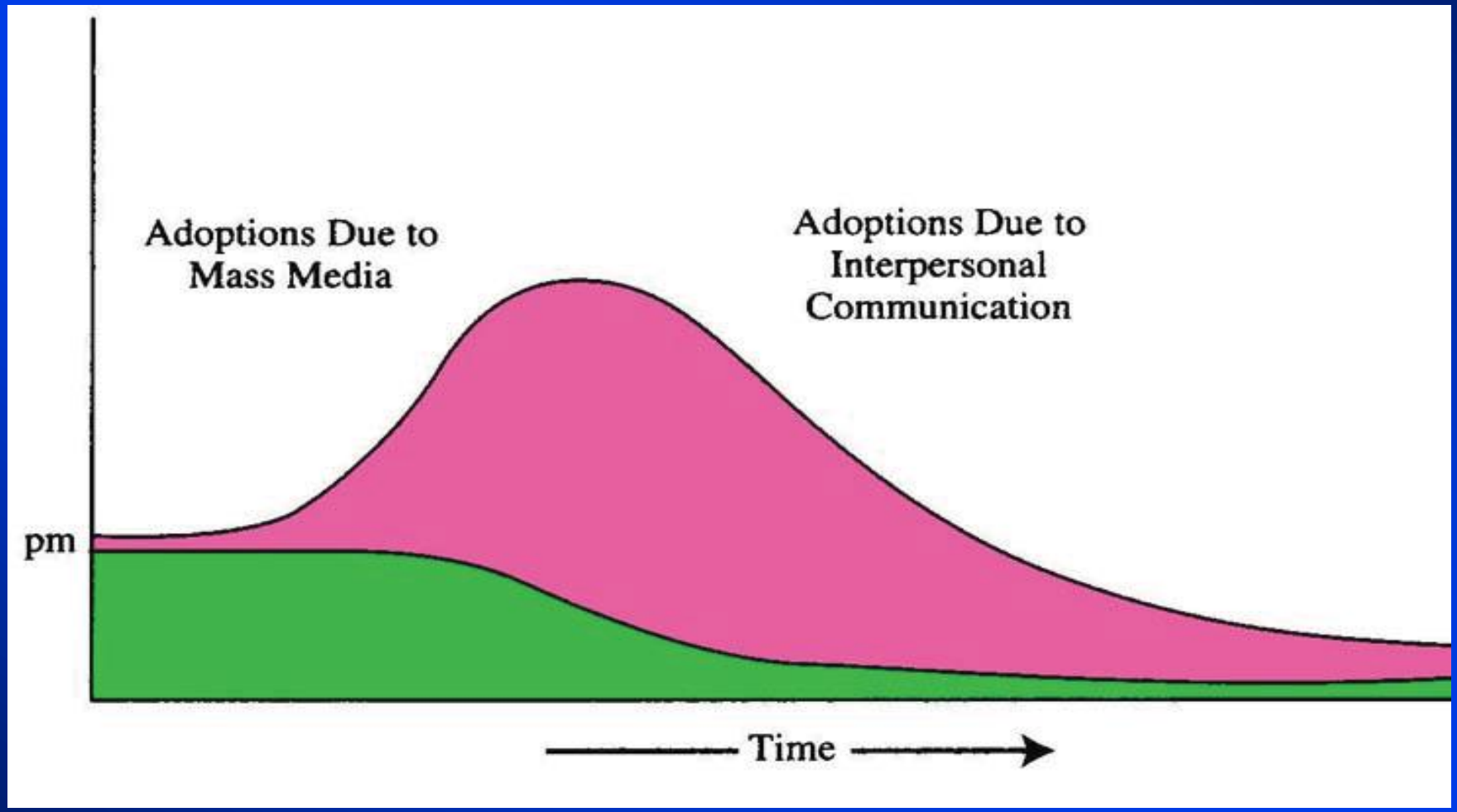
- the science and evidence-base for use of toxicogenomics in human health risk assessment (led by WHO) and issues of relevance to human health and linking with existing work on biomarkers, modes-of-action and ethical considerations; and
- the other on defining the needs and possible application of toxicogenomics in a regulatory context.

# ***Leadership Roles – Change Agent as Innovators?***




***Source: Rogers, E.M. (2003). Diffusion of Innovation Theory***

# Leadership Roles – Change Agent and Adaptation




*Source: Mahajan, Muller and Bass (1990) as reproduced in Rogers, E.M. (2003) p210. Bass Forecasting Model*

# *Leadership Roles in Galatians 1-6*

**To be free is not merely to cast off one's chains, but to live in a way that respects and enhances the freedom of others.**

**Nelson Mandela**

NCHPEG
National Coalition for Health Professional Education in Genetics



# Tools and Downloads

## Downloads

Print-version of the Core Principles in Family History

Core Principles in Family History Quick Facts: This one-page PDF document is a useful quick reference or handout for educators and trainees.

## Medical Family History: Tools for Your Practice

PRINCIPLES FOR FAMILY HISTORY

Rationale

Principles for Collection

Principles for Interpretation

Principles for Intervention

Purpose and Limitations