

The Importance of Educating Asian Patients About their Clinical Lab Test Results

18th Conference on Healthcare of the Chinese in
North America

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Alan H. Wu, Ph.D.

Clinical Chemistry Lab Director

San Francisco General Hospital

Why do you need to take control of your medical lab information?

- 70% of all medical decisions based on results of clinical lab tests
- 95% when radiology, biopsies, ECGs, stress tests, etc. are included
- 99.9% of the public don't understand the effort to ensure a quality lab result.
- Medical mistakes account for 100,000 deaths/y, 3rd behind heart disease and cancer

Nation & World: Tuesday, November 30, 1999

Study: 98,000 deaths each year are linked to medical mistakes

by Rick Weiss
The Washington Post



How does this happen?

- Inappropriate selection or dosing of drugs producing unexpected side effects
- Mistakes made in the interpretation of clinical lab data
- Faulty medical devices
- Human error
- Failure of patients/families to seek second opinion

The changing dietary paradigm

- We organic produce
- We study nutritional labels
- We avoid GMO products



Nutrition Facts	
Serving Size 1 cup (200g)	
Amount Per Serving	
Calories 260	
	% Daily Value
Fat 13g	20%
Saturated Fat 3g	25%
+ Trans Fat 2g	
Cholesterol 30mg	10%
Sodium 660 mg	28%
Carbohydrate 31g	10%
Fiber 0g	0%
Sugars 5g	
Protein 5g	
Vitamin A 4%	Vitamin C 2%

Key question

- If we are so interested in what we put into our body, why are we NOT interested in what is being done to our body?



What can I do?



- Review your own medical information.
- Clinical laboratory data available on line from providers.
- Understand the basis behind the medical decision to be made
- Understand how the laboratory works and what can happen when mistakes are made

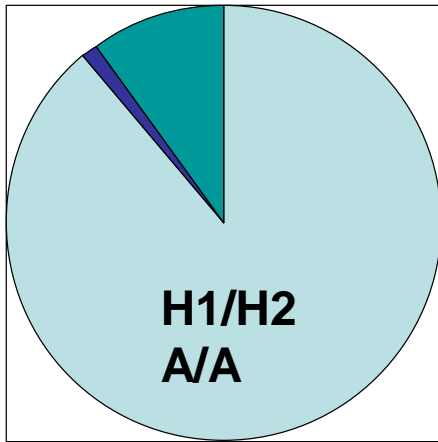
Disorders more relevant for Chinese

- Genetic variances: pharmacogenomics
- Liver cancer and hepatitis

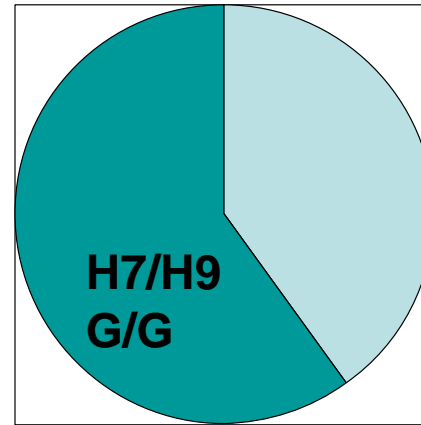
Warfarin



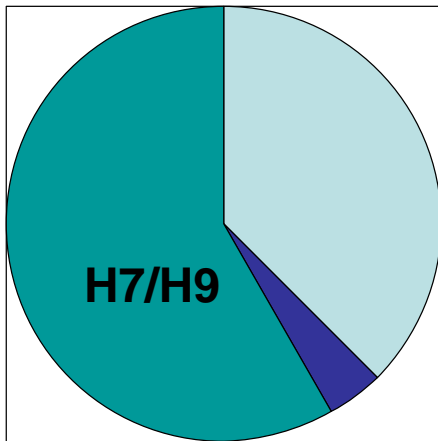
Ethnic variation for VKORC1: UCSF data



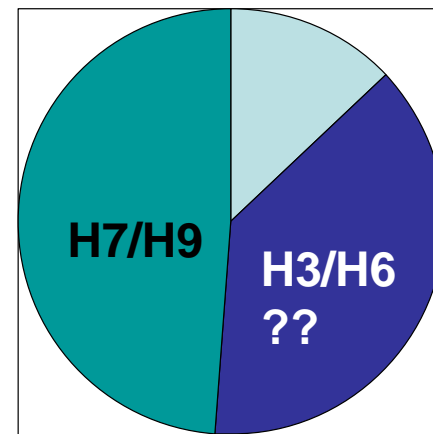
Asians



Hispanic



Whites



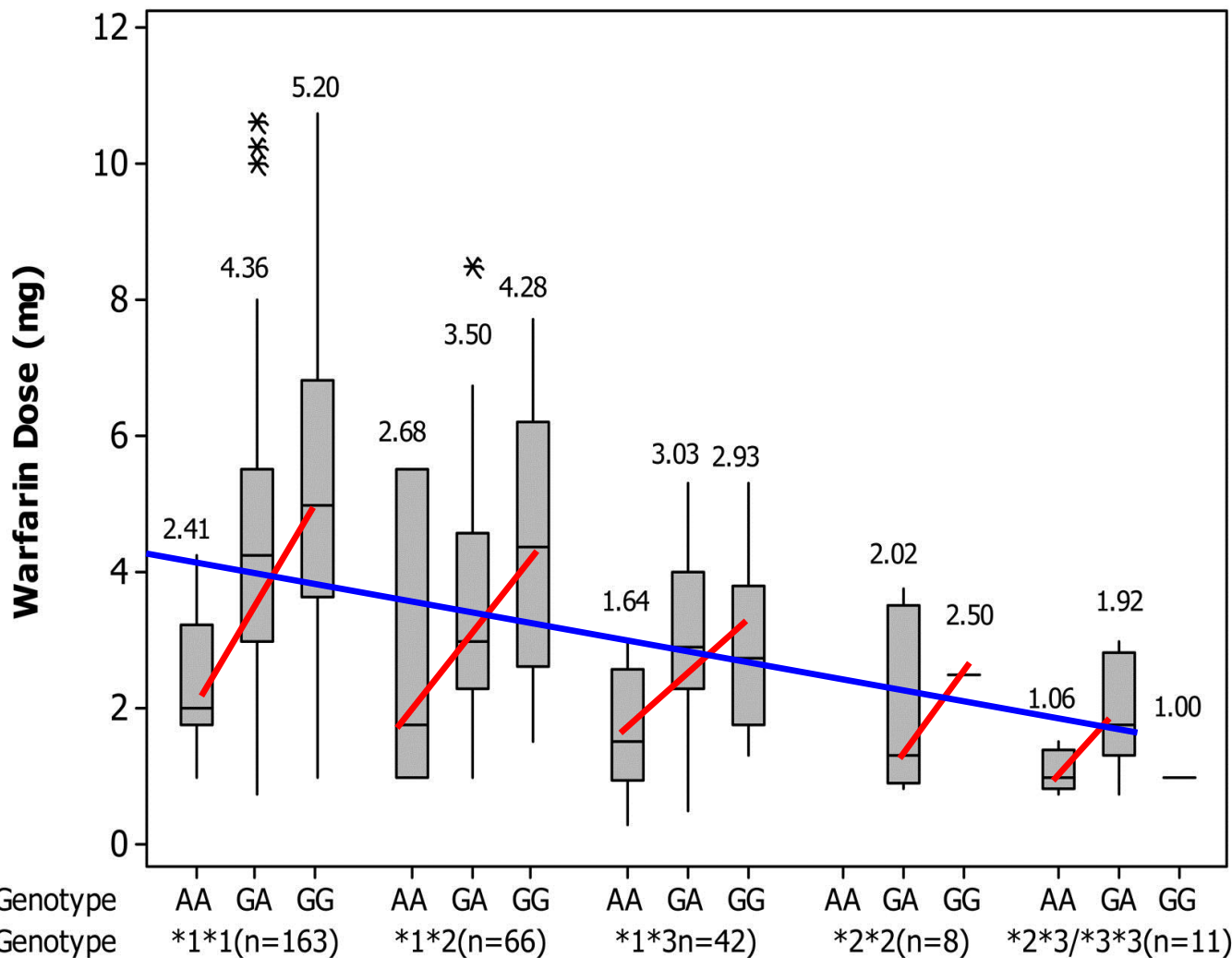
African American

Pharmacokinetics + pharmacodynamics

Sconce et al. Blood 2005;106:2329-33.

- *2/*3: low dose
- *1: high dose
- -1639 A: low dose
- -1639 G: high dose

→ *VKORC1* Genotype
→ *CYP2C9* Genotype



WARFARIN DOSING

www.WarfarinDosing.org

> [Warfarin Dosing](#)

> [Clinical Trial](#)

> [Outcomes](#)

> [Hemorrhage Risk](#)

> [Patient Education](#)

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User:

Patient:

Required Patient Information

Age: 55 Sex: Male Ethnicity: Non-Hispanic

Race: African American or Black

Weight: 176 lbs or 80 kgs BSA 1.88

Height: (5 feet and 5 inches) or (165.1 cms)

Smokes: Yes Liver Disease: No

Indication: Atrial fibrillation

Baseline INR: 1 Target INR: 2 Randomize & Blind

Amiodarone/Cordarone® Dose: mg/day

Statin/HMG CoA Reductase Inhibitor: Atorvastatin/Lipitor®/Caduet®

Any azole (eg. Fluconazole): No

Sulfamethoxazole/Septera/Bactrim/Cotrim/Sulfatrim: Yes

Genetic Information

VKORC1-1639/3673: AG

CYP4F2 V433M: CT (heterozygous)

GGCX rs11676382: GG (homozygous mutant)

CYP2C9*2: CC (wildtype)

CYP2C9*3: AC (heterozygous)

CYP2C9*5: GG (homozygous mutant)

CYP2C9*6: AA (wildtype)

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> ESTIMATE WARFARIN DOSE

WARFARINDOSING

www.WarfarinDosing.org

Estimate of Warfarin Dose

Estimated [mini-loading dose](#): 2.5 mg for initial warfarin dose.*

Estimated therapeutic dose: 1.7 mg/day.

*To have the INR rise quickly, prescribe ~50% more than the mini-loading dose (e.g., 3.5 mg) for the initial 1 or 2 days.

[Click here](#) to get an IWPC estimate.

Today's prescribed dose:



(Slide the Pointer to the dose you would like to prescribe today.)

Patient Code (e.g. TestABC or 007) :

Email address to save patient under :

When would you like an email to remind you to check the INR: In hours.

All information entered into this site is kept confidential. Your e-mail address will not be shared, sold, or rented. It is required to save and to access this record.

Recommendations

> [Warfarin Dosing](#)

> [Outcomes](#)

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User:

Patient: 0

Version 17.4

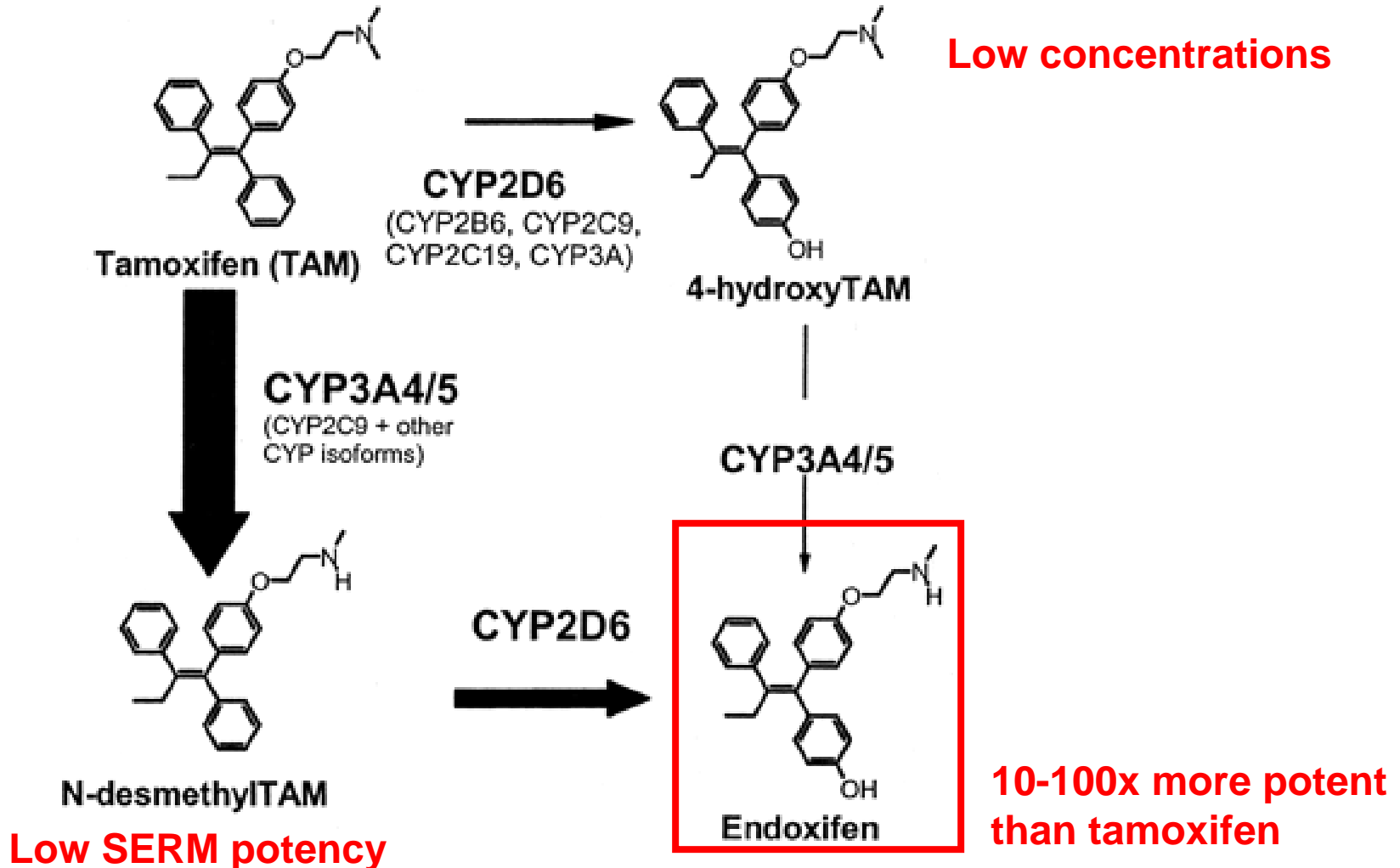
Build : June 29, 2009

Tamoxifen



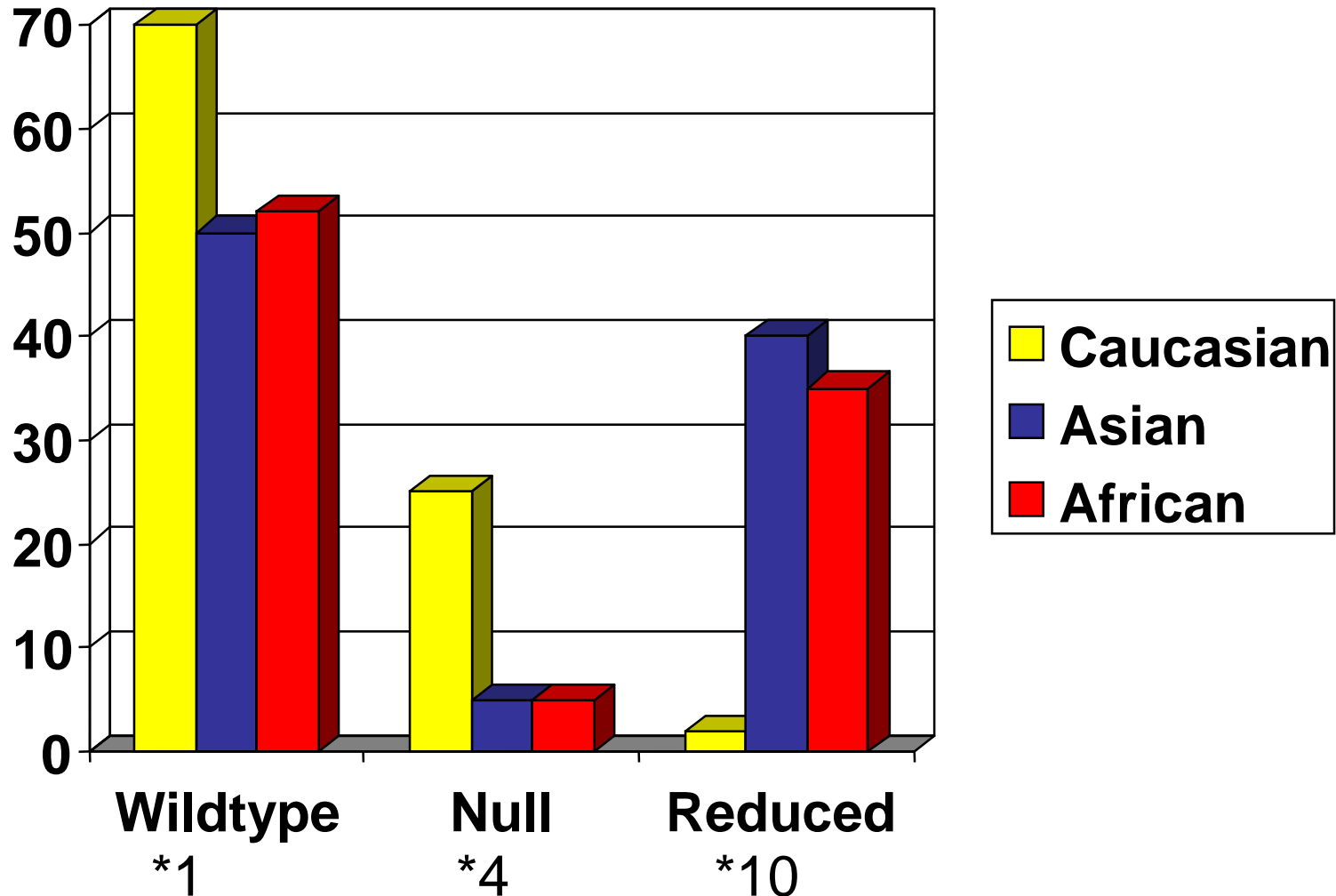
Metabolism of tamoxifen

Jin et al. J Nat Can Inst 2005;97:30-9.



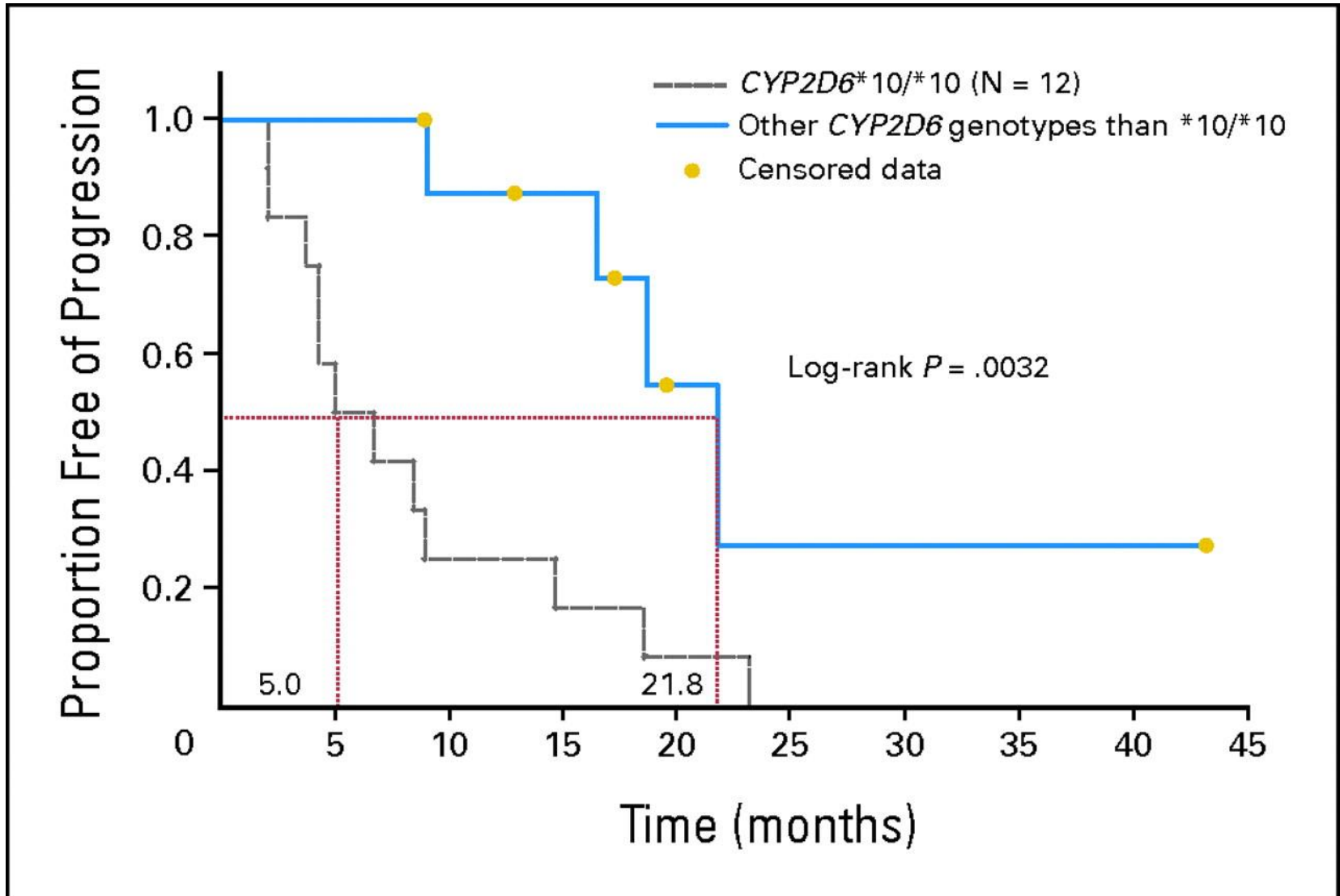
CYD 2D6 allele frequencies

Bradford et al. Pharmacogen 2002;3:229-43.

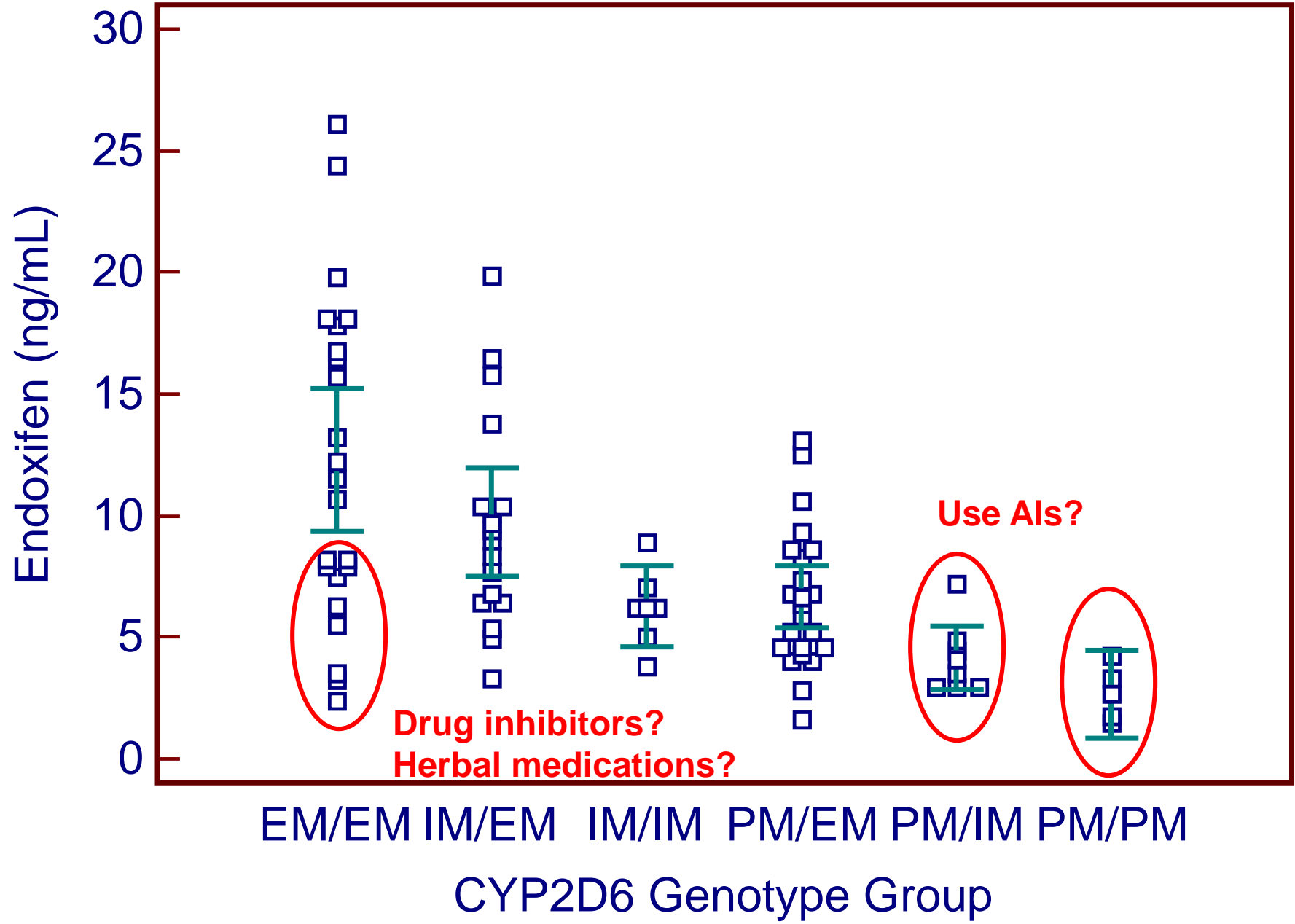


Tamoxifen therapy and 2D6 *10

Lim et al. J Clin Oncol 2007;25:3837-45.



Endoxifen Concentration by CYP2D6 Genotype Group

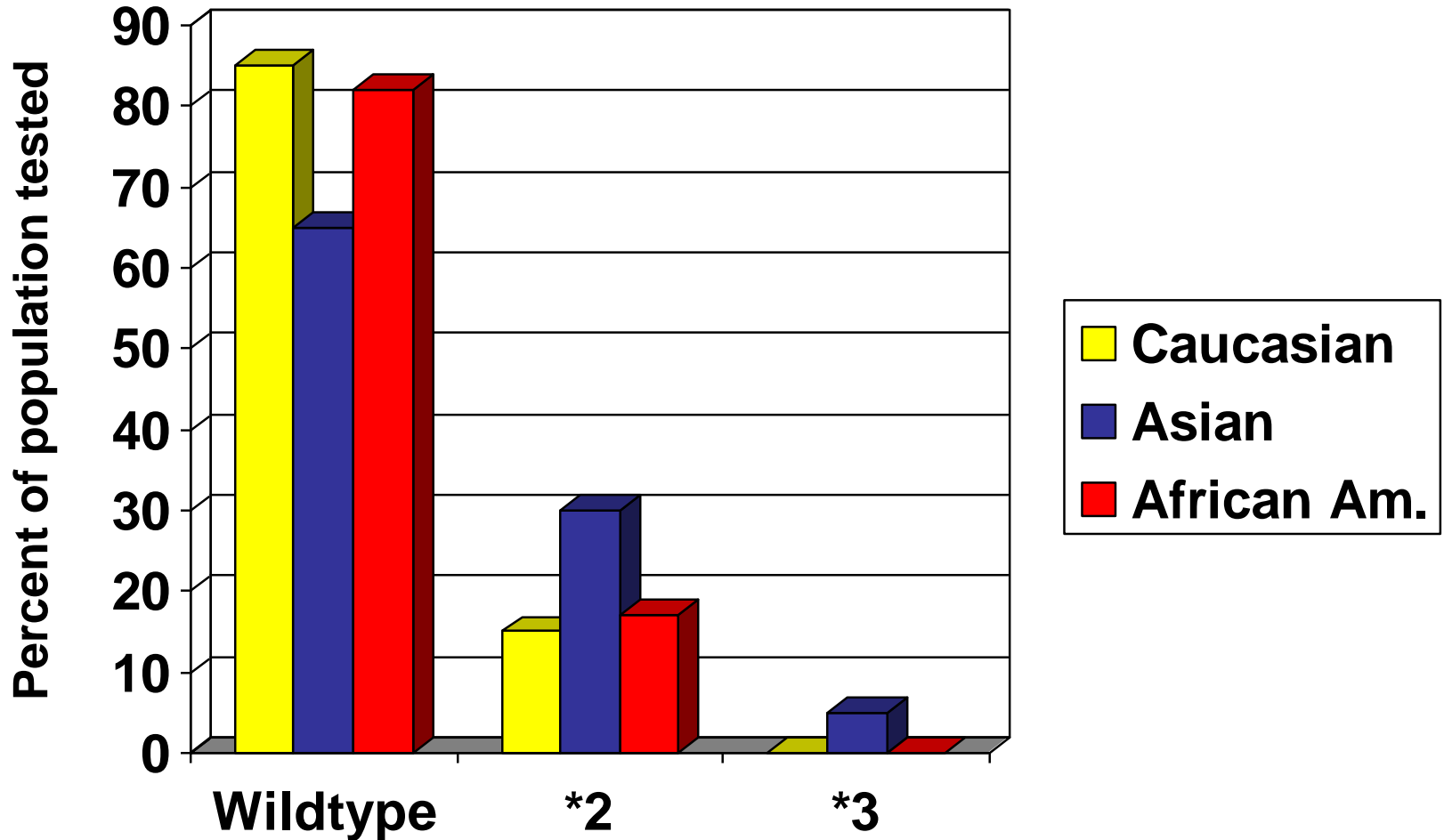


Clopidogrel



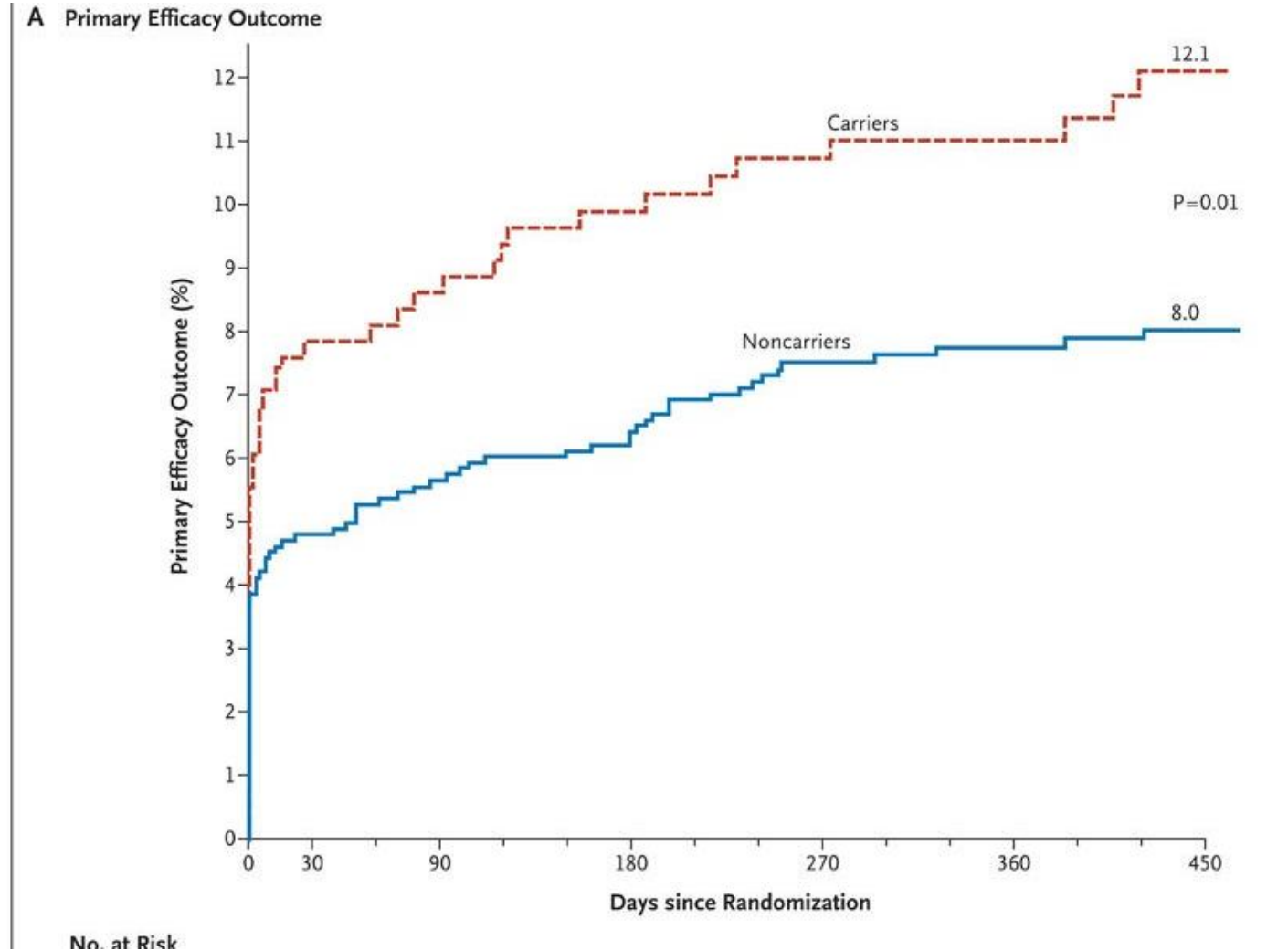
CYD 2C19 allele frequencies

Xie et al. Ann Rev Pharmacol Toxicol 2001;41:815-50



PGx of clopidogrel

Mega et al. NEJM 2009;360:354-62.



Editorial

For reprint orders, please contact: reprints@futuremedicine.com

The Hawaii clopidogrel lawsuit: the possible effect on clinical laboratory testing

“...citizens are paying 100-times more than aspirin for an ineffective drug.”

Keywords: [clopidogrel](#) • [CYP2C19](#) • [slow metabolizers](#)

Rudy was a fourth-generation fisherman (name changed). His great grandfather came over from a Polynesian island a half century before Hawaii became the 50th state of the

and an ambulance was called. It appeared that he was suffering an acute myocardial infarction (AMI).

It was cases like this that prompted District

Personalized Medicine



Pharmacogenomics for reducing incidence of Stevens Johnson Syndrome



Prospective clinical trial of HLA-B 1502

Chen et al. NEJM 2011;364:1126-33.

Table 3. Historical Incidence of Carbamazepine-Induced SJS–TEN in 2002, 2003, and 2004, as Compared with the Incidence among Study Subjects.*

Variable	2002	2003	2004
New recipients of carbamazepine (no.)	50,917	48,522	49,670
Subjects with ICD-9-CM diagnostic code 695.1 (no.)	1441	1261	1354
Carbamazepine-induced SJS–TEN (no.)	123	108	116
Incidence of carbamazepine-induced SJS–TEN (%)	0.24	0.22	0.23
P value for comparison between historical incidence and incidence among study subjects†	<0.001	<0.001	<0.001

Drug-Induced Hypersensitivity Reactions

Stevens-Johnson Syndrome / Toxic Epidermal Necrolysis



Medications commonly implicated:

anti-gout agents

Antibiotics

antipsychotics

antiepileptics

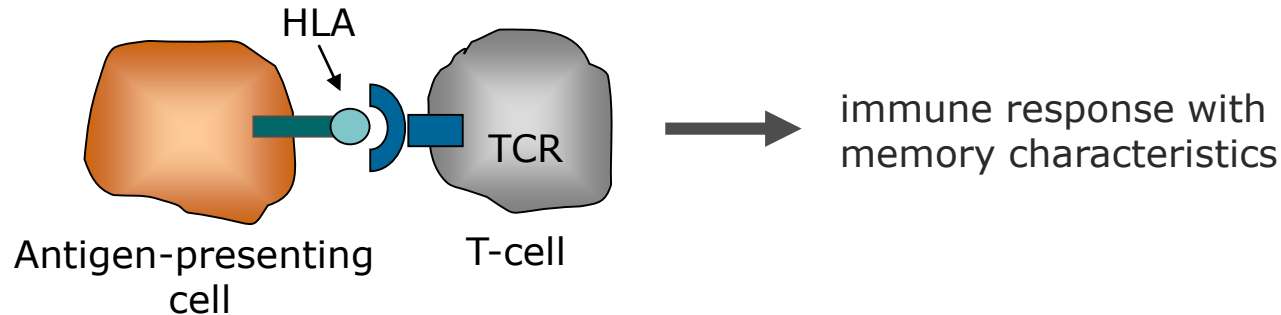
analgesics

NSAIDS



Genetic Association between HLA and drug hypersensitivity

Human Leukocyte Antigen (HLA) = Human Major Histocompatibility Complex (MHC)



Drug	Drug Class	HLA type
	Sulfonamides	HLA-A29, HLA-B12, HLA-DR7
Ximelagatran	Anti-coagulant	HLA-DRB1*07, HLA-DQA1*02
Methazolamide	Diuretic (ocular conditions)	HLA-B59
Oxicam	NSAID	HLA-A2, HLA-B12
Carbamazepine	Anti-epileptic	HLA-B*1502
Allopurinol	Uricosuric (for treatment of gout)	HLA-B*5801
Abacavir	Anti-retroviral	HLA-B*5701

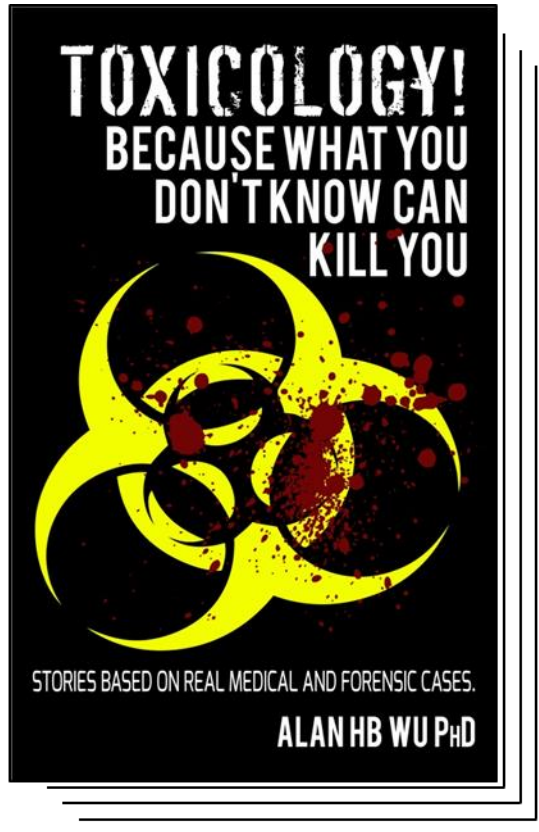
HLA-B*1502 and Carbamazepine: odds ratio 2504 (South-eastern Asians)

HLA-B*5801 and Allopurinol: odds ratio 580 (Han Chinese)

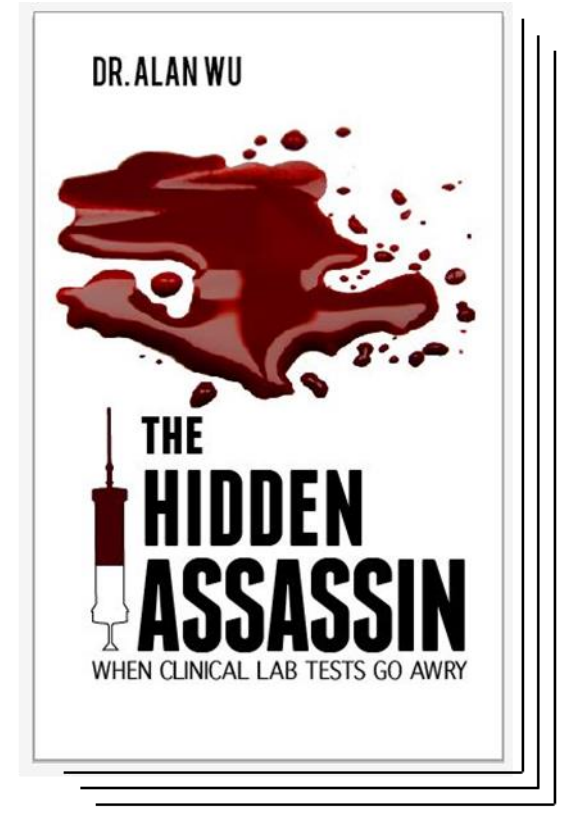
~~HLA-B*5701 and Abacavir: odds ratio 960 (Caucasian)~~

Paperbacks with real stories

Available through:
www.alanhbwu.com/



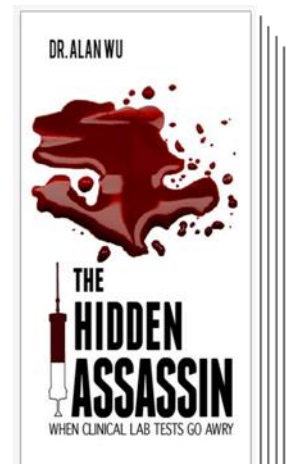
*Tox testing that solved
forensic cases*



*Clin lab tests that solved cases
or caused harm*

Dangers of warfarin

- A Chinese real estate agent develops atrial fibrillation
- Her doctor says, ***“I will take care of you”***
- She’s given 5 mg warfarin. A few weeks later, she suffers a debilitating stroke
- Pharmacogenomic lab analysis: 2C9 *2/*3, VKORC1 AA genotype
- 1 mg was her optimum dose
- This was a “A fib about afib”



Pilot 2013 PGx study: Testing of UCSF Pharmacy students



Volunteers sought. Consent form signed. IL28b and other genes tested

Bottom Up

We found Freda was a 2C19 *2/*2 and at risk for a thrombosis following a stent. During summer break, her father suffers a heart attack and is scheduled for emergent angioplasty. Following implantation, the cardiologists puts him on 75 mg Plavix.

Freda, knowing that he likely carries at least one *2 variant, tells the MD about 2C19 Pgx. He says:

“Pharmacogenomic testing is not standard practice here. We follow standard protocols established by this hospital and medical practice.”

The doctor was visibly annoyed that a pharmacy student was telling him how to manage his patient.

1 month later, Freda’s dad died of a 2nd AMI.

