

GM¹⁰



Pharmacogenomics

Genomic Medicine

U.S. News & World Report
JANUARY 20, 2003 www.usnews.com

THIS DRUG'S FOR YOU

NEW TARGETED MEDICINES PROMISE BREAKTHROUGH CURES



PARADE

Take Charge Of Your Health

Just Your Ordinary Company Says "No!"

Get Medical Care Without Getting Sick

A Homestead of Food Lovers

500 Best Places to Live

24 October 2003
Science
Vol. 302 No. 5645
Pages 517-728 \$10

JANUARY 13, 2003 \$3.50 www.time.com AOL Research TIME

TIME SPECIAL ISSUE

DRUGS OF THE FUTURE

Amazing new medicines will be based on **DNA**

Find out how they will change **YOUR LIFE**

Genomic Medicine

THE ADVANCEMENT OF SCIENCE



Changing medicine: Liggett with DNA sequence

Prescription for Disaster

Every year, more than 100,000 people die in the U.S. because they carry "misspelled" genes that lead to deadly diseases. Now doctors are using DNA sequence to identify ineffective prescribing.

Newsweek

nature insight

human genomics and medicine

Pharmacogenetic Testing in Psychiatry: Not (Quite) Ready for Primetime

Robert H. Howland, MD

Journal of Psychosocial Nursing and Mental Health Services

November 2014 - Volume 52 · Issue 11: 13-16

- COUNTERPOINT -

Pharmacogenetic-Based Initial Dosing of Warfarin: Not Ready for Prime Time

Charles S. Eby^{1*}

Anesthesia and Pharmacogenomics: Not Ready for Prime Time

Keith Candiotti, MD

The age of interindividualize
Pharmacogenomics has

The NEW ENGLAND JOURNAL of MEDICINE

[Pharmacoeconomics](#). 2006;24(12):1173-7.

Do pharmacogenomic tests provide value to policy makers?

Shih YC, Pusttai L.

EDITORIAL



Pharmacogenomics — Ready for Prime Time?

Susan B. Shurin, M.D., and Elizabeth G. Nabel, M.D.

Clinical reviews in allergy and immunology

Pharmacogenomics and adverse drug reactions: Primetime and not ready for primetime tests

David A. Khan, MD Dallas, Tex

Perspectives

Pharmacogenetics in the Management of Coumarin Anticoagulant Therapy: The Way Forward or an Expensive Diversion?

Mike Greaves

Zhou, J *J Pharmacogenom Pharmacoproteomics* 2012, 3:5
<http://dx.doi.org/10.4172/2153-0645.1000e126>



Pharmacogenomics & Pharmacoproteomics

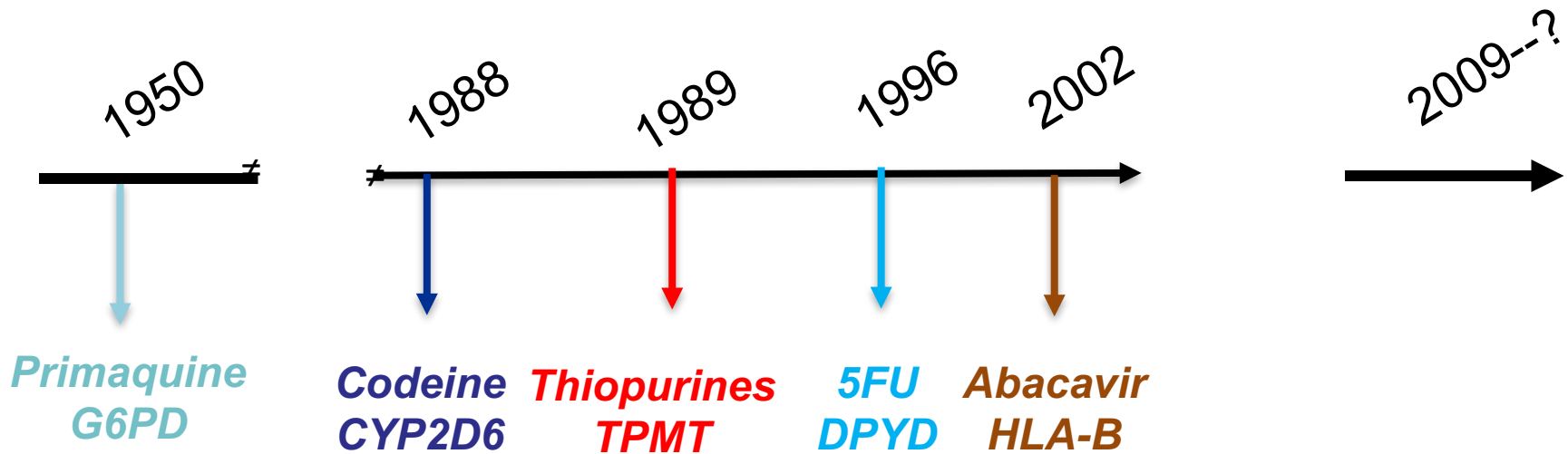
Editorial

Open Access

Is Pharmacogenomics Ready for Prime Time?

Shu-Feng Zhou*

Actionable pharmacogenetic gene/drug pairs have been known for a long time...
use in the clinic still rare



GMX Objectives

- Survey national landscape of research programs in pharmacogenomics implementation
- Review current advances and clinical applications of pharmacogenomics implementation
- Discuss limitations and obstacles in pharmacogenomics clinical implementation
- Identify evidence gaps and studies that are needed to address them
- Design strategies for large-scale evaluation and implementation of pharmacogenomics in clinical care in the U.S.

Session 6: Role of NHGRI and the Genomic Medicine Community in PGx Implementation Research

Moderator: **Laura Rodriguez**
NIH/NHGRI

1:30 p.m.	Summary and Synthesis	Teri Manolio NIH/NHGRI Mary Relling St. Jude Children's Research Hospital
2:30 p.m.	Next Steps	
3:00 p.m.	Meeting Adjourn	

Summary of pre-GMX meeting survey

- Sent to CPIC implementers, eMERGE, ClinGen, IGNITE
- 36/73 (49%) responded
- 64% were university/academic/NIH
- Clinical vs research
 - 58% both clinical and research
 - 27% clinical only
 - 15% research only
- Reactive (51%) vs preemptive (49%)
- Many different genotyping platforms
- 63% have/are/will file for 3rd party reimbursement

Pre-GMX survey: External resources used by implementers

34	Clinical Pharmacogenetics Implementation Consortium (CPIC)
28	PharmGKB
7	IGNITE Spark
6	ClinVar
4	Dutch Pharmacogenetics Working Group
2	FDA
2	St Jude-PG4KDS webpage
2	PGRNSeq
1	Other resources mentioned once:

CDS-KB; BioVU; Medial Package Inserts and analysis of peer-reviewed journal articles; OneOme proprietary that integrates from CPIC, PharmGKB, ClinVar and primary literature; DIGITizE; YouScript; Vanderbilt webpage; Paid consultant from NorthShore in Chicago; TPMT alleles website; U of Illinois Website; CYP alleles website; UGT Alleles website; dbSNP; Medical College of Wisconsin Development lab; CBioportal; COSMIC; PUBMED; MYCANCER GENOME; OMIME EXOME Variant Server; Genetic Testing registry; EMA; SPCs; ACMG guidelines; EU Horizon 2020 Program; NCBI

Pre-GMX survey: Gene/drug pairs implemented

32	CYP2C19-clopidogrel	Others:
30	SLCO1B1-simvastatin	
29	CYP2C9/VKORC1-warfarin	CYP2C9-phenytoin
28	TPMT-thiopurines	CYP2C19-PPIs
26	CYP2D6-codeine	CYP2C19-voriconazole
25	Antidepressants and CYP2C19 &/or CYP2D6	CYP2D6-tramadol x 2
21	DPYD-fluorouracil, capecitabine	CYP3A5-tacrolimus x 2
15	UGT1A1 and specific drugs (Irinotecan, belinostat, nilotinib, pazopanib, atazanavir, erlotinib, indacaterol, abacavir)	Proprietary multi-gene algorithm applies CYP to other known substrates; NUDT15 and selection of informative genes
14	IFNL3-ribavarin, peginterferon	Somatic variations up to 313 gene drug pairs in cancer treatment
12	HLAB-abacavir	IL28B, CYP3A5, CYPB26
11	HLA and other drugs (allopurinol, carbamazepine, phenytoin)	CYP2D6-other opiates beyond codeine
		G6PD-rasburicase
		NGS sequencing for somatic mutations (KRAS, BRAF, ALK, EGFR, ROS1, PD1) for oncology
		CYP2D6/Ondansetron

Pre-GMX Survey Challenges/Obstacles

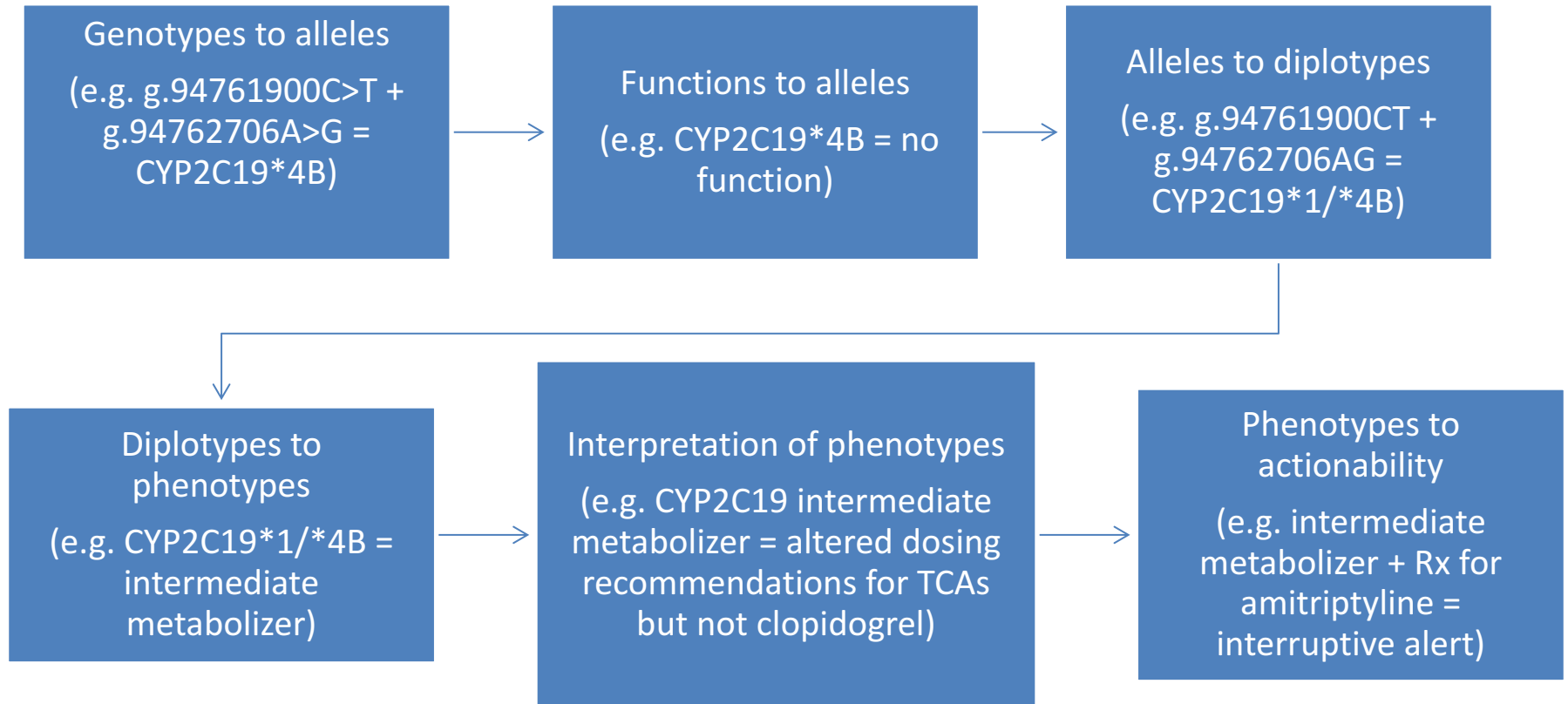
- LACK OF FUNDING, TEST REIMBURSEMENT
- LACK OF INSTITUTIONAL SUPPORT
- CHALLENGES WITH IT/EMR/CDS
- LABORATORY/GENOTYPING TECHNOLOGY
- LACK OF EDUCATION OF CLINICAL STAFF, PTS
- LACK OF CLINICIAN BUY-IN

Sessions addressing each of these
issues over the next 1.5 days

Distinctions: research vs implementation

- Pharmacogenetic **research**
 - Test whether variants are related to phenotypic variation in drug activity or PK (in vitro, pre-clinical)
- Clinical pharmacogenetic **research**
 - Test whether variants are related to phenotypic variation in drug response in patients
- Clinical pharmacogenetic **implementation research**
 - Test questions related to processes related to clinical pharmacogenetic implementation (e.g. randomized studies of testing, education, EHR use, payment success, test types, clinician performance/adherence, cost effectiveness, etc)
- Clinical **implementation** of pharmacogenetics
 - For genetic variants/drugs that are already clinically validated, the “research” is “done” but the implementation still requires **resources**

The process to go from genotype to prescribing can be complicated



<https://cpicpgx.org/guidelines/>

<https://www.pharmgkb.org/page/cyp2c19RefMaterials>

FILE HOME INSERT PAGE LAYOUT FORMULAS DATA REVIEW VIEW

Clipboard Font Alignment Number Styles Cells Editing

Calibri 11 A A Wrap Text Custom

B I U Merge & Center \$ % .00 .00 Conditional Formatting Table

Normal Bad Good Neutral

AutoSum Fill Clear Sort & Filter

	A	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T
5																
6	Drug	Fluoxetine	Paroxetine	Simvastatin	Ondansetron	Oxycodone	Clopidogrel	Fluoropyrimidines	Amitriptyline	Atazanavir	Voriconazole	Tacrolimus	Tamoxifen	Pimozide	Methadone	Efavirenz
7	Gene	CYP2D6	CYP2D6	SLCO1B1	CYP2D6	CYP2D6	CYP2C19	DPYD	CYP2D6 and CYP2C19	UGT1A1	CYP2C19	CYP3A5	CYP2D6	CYP2D6	CYP2B6	CYP2B6
8	Adverse Outcomes	Increased toxicity or therapeutic failure	Increased toxicity or therapeutic failure	Myopathy	Poor IV control	Increased toxicity or therapeutic failure	Increased or reduced platelet inhibition	Increased toxicity	Increased toxicity or therapeutic failure	Hyperbilirubinemia	Increased toxicity or therapeutic failure	Lower blood concentrations				
9	Implementation Status	Live	Live	Live	Live	Live	Live	Live	Live	Live	Live	Live				
10	Clinical impact of negative outcomes significant	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
11	Scientific evidence for drug gene effect	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
12	Patient target identifiable before they receive drug	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
13	Alternative therapy available	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
14	Gene added to DMET tracker	✓	✓	Oct-12	✓	✓	Apr-13	May-14	✓, Apr-13	Oct-14	Apr-13	Apr-15				
15	DTA for new gene created															
16	Gene specific look up tables created	Aug-11	Aug-11	May-13	Aug-11	Aug-11	Jul-13	Apr-14	Aug-11, Jul-13	Oct-14	--	Apr-15				
17	Gene added to consult builder											Jan-16				
18	Consult template written	✓	✓	✓	--	--	Jul-13	May-14	Aug-11, Jul-13	Nov-14	--	Jan-16				
19	Problem List Entries created											Dec-15				
20	Consult database updated	✓	✓	✓	--	--	Jul-13	May-14		Dec-14	--	Jan-16				
21	CDS language developed	Jun-12	Jun-12	Nov-12	Feb-13	Feb-13	Jun-13	May-14	Jun-12, Jun-13	Apr-15	Apr-15	Jan-16				
22	Dose Range Checking Alerts Modified (if applicable)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Sep-15	Jan-16				
23	Power Plans Updated (if applicable)											N/A				
24	Patient result letters	✓	✓	✓	--	--	Jul-13	Jun-14	✓, Jul-13	Apr-15	--	Mar-16				
25	Gene specific "Do you Know..." sheet	Feb-12	Mar-12	Feb-13	--	--	Jul-13	May-14	Jan-12, Jul-13	Feb-15	--	Mar-16				
26	Patient medication card updated	✓	✓	N/A	✓	Jul-13	--	May-14	✓, --	Dec-14	--	Dec-16				
27	PGEN formulary table updated	Mar-13	Mar-13	May-13	Mar-13	May-13	Jun-13	May-14	N/A	Apr-15	--	Mar-16				
28	Drug monograph updated in formulary	Mar-13	Mar-13	N/A	Mar-13	May-13	N/A	May-14	Mar-13	Jun-15	--	Mar-16				
29	St Jude PG4KDS webpage updated	Jun-11	Jun-11	May-13	Feb-13	May-13	Jul-13	May-14	Aug-14	Apr-15	--	Mar-16				
30	Inform Portal Team to add new gene letters															
31	Gene/Drug pair updated in email notification table															
32	Staff education	✓	✓	Jun-13	✓	Jun-13	Jun-13	May-14	Aug-14	May-15	--	Mar-16				
33	Competencies*	Oct-12	Oct-12	Jun-13	Feb-13	Jan-15	Jul-13	Jun-14	Jan-15	Apr-15	--	Apr-16				
34	P & T Communication	✓	✓	✓	✓	✓	Jul-13	Jun-14	Jul-14	Apr-15	Apr-15	Mar-16				
35	POC Communication	Jul-11	Jul-11	Jun-13	Mar-13	Mar-13	Jun-13	May-14	Jun-14	Apr-15	Apr-15	Apr-16				
36	Go-Live Date	5/30/2012	5/30/2012	5/15/2013	2/28/2013	5/15/2013	6/14/2013	5/20/2014	8/15/2014	4/24/2015	7/10/2015	3/8/2016				
37																
38	Note: The items listed above are not checked off in sequential order.															
39	* refers to the date that the competencies were created															

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