



VANDERBILT UNIVERSITY
MEDICAL CENTER

Engineering healthcare systems to deliver genomic medicine

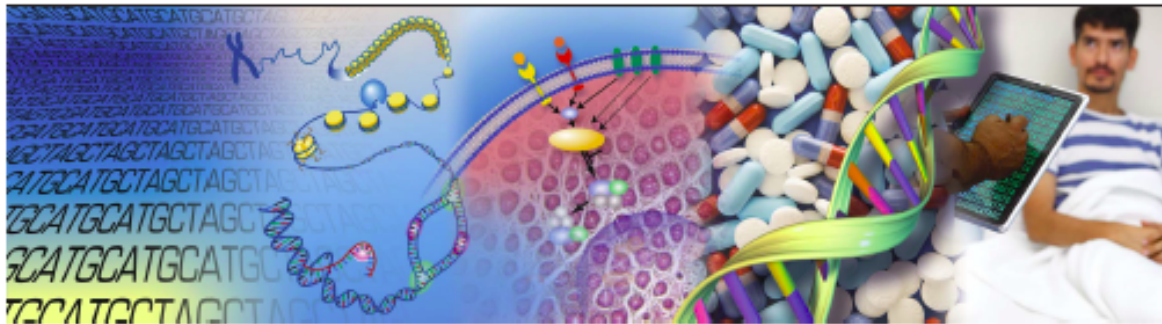
Dan M. Roden, MD

Assistant Vice Chancellor for Personalized Medicine

Vanderbilt University School of Medicine

Domains of genomic research

Understanding the Structure of Genomes	Understanding the Biology of Genomes	Understanding the Biology of Disease	Advancing the Science of Medicine	Improving the Effectiveness of Healthcare
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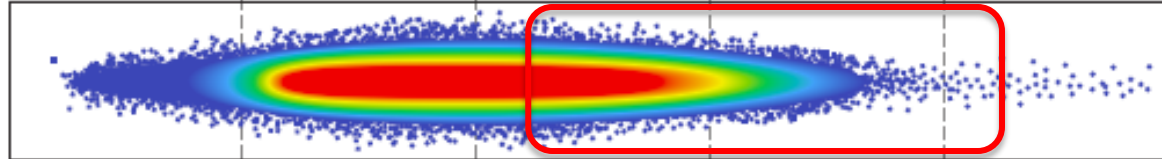
1990-2003
The Human Genome Project



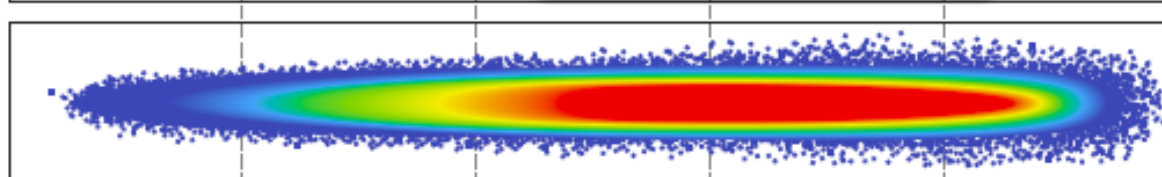
2000-2010

- Genomic predictors of disease susceptibility and drug response
- Engaging the Electronic Medical Record (EMR) for discovery

2011-2020

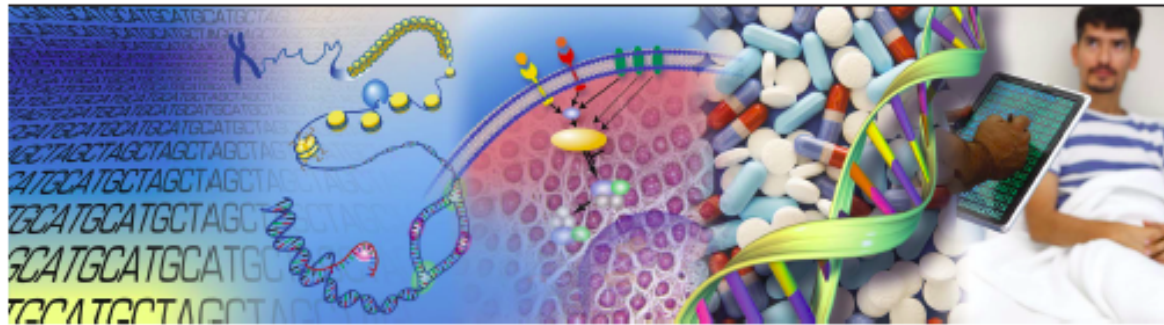


Beyond 2020



Domains of genomic research

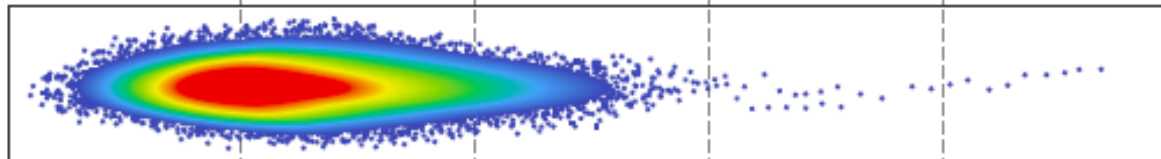
Understanding the Structure of Genomes Understanding the Biology of Genomes Understanding the Biology of Disease Advancing the Science of Medicine Improving the Effectiveness of Healthcare



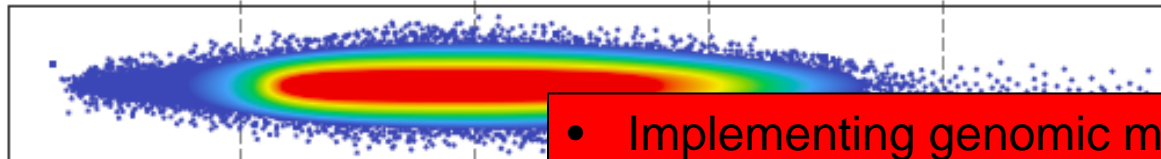
1990-2003
The Human Genome Project



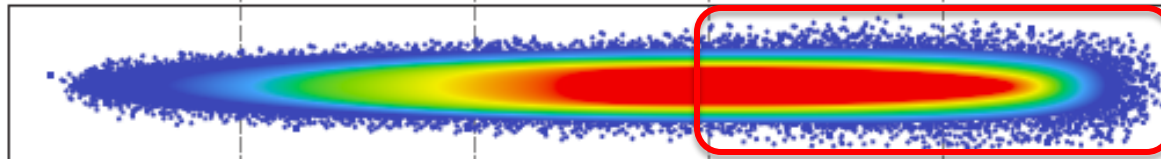
2000-2010



2011-2020



Beyond 2020



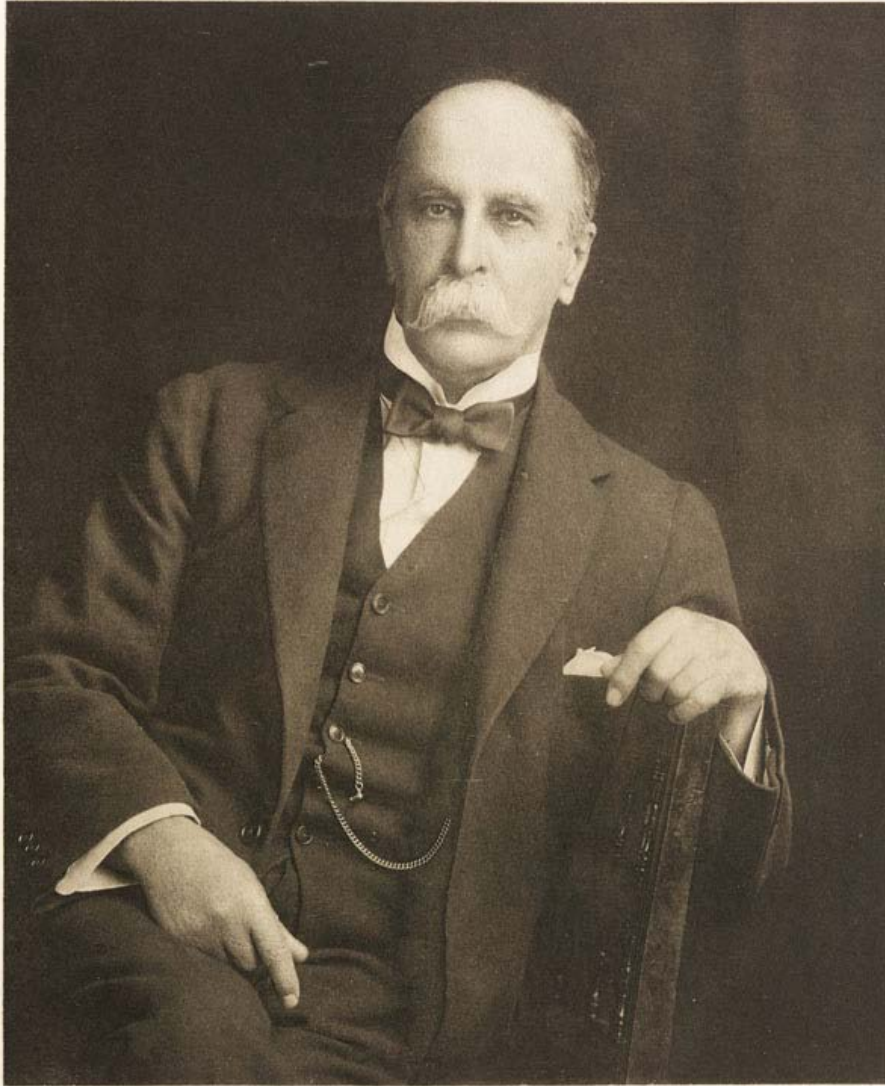
• Implementing genomic medicine

One working definition of Genomic Medicine

NHGRI's Genomic Medicine Working Group

- An emerging medical discipline that involves using genomic information about an individual as part of their clinical care (e.g., for diagnostic or therapeutic decision - making) and the other implications of that clinical use.

Personalized medicine – not a new idea



The good physician treats the disease; the great physician treats the patient who has the disease.

Sir William Osler

The vision



"Here's my sequence..."

New Yorker, 2000

Collins: Pharmacogenomics will undoubtedly become a very compelling part of medical practice. The limiting factor right now is that oftentimes, if you are ready to write a prescription, you do not want to wait a week to find out the genotype before you decide whether you've got the right dose

and the right drug. But if everybody's DNA sequence is already in their medical record and it is simply a click of the mouse to found out all the information you need, then there is going to be a much lower barrier to beginning to incorporate that information into drug prescribing. If you have the evidence, it will be hard, I think, to say that this is not a good thing. And once you've got the sequence, it's not going to be terribly expensive. And it should improve outcomes and reduce adverse events.

How will this vision actually start to be tested and become reality?



"Here's my sequence..."

New Yorker, 2000

Excellence in
biomedical
sciences

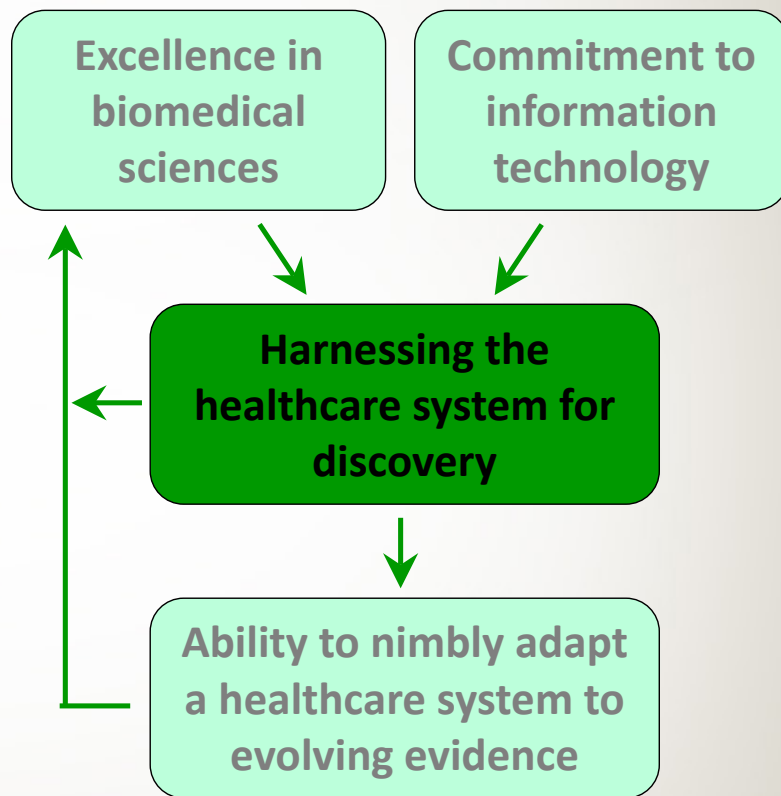
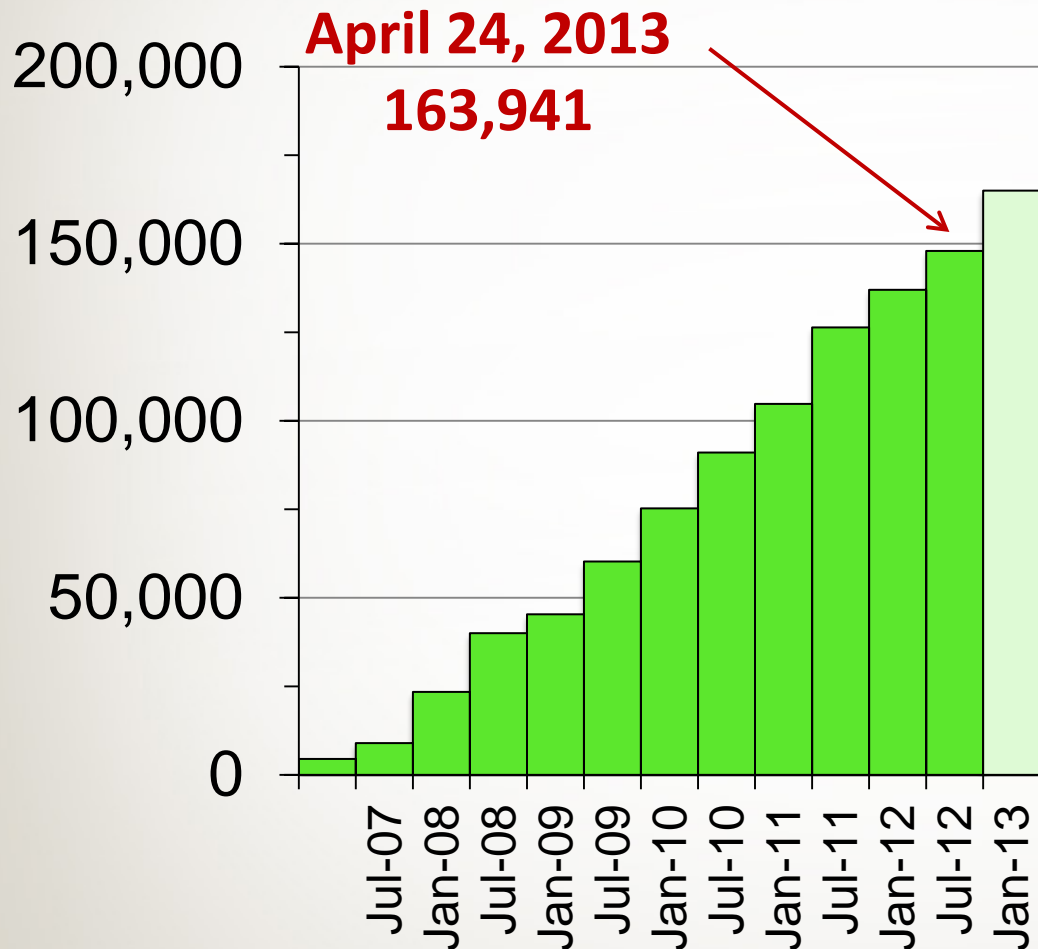
Commitment to
information
technology

Harnessing the
healthcare system for
discovery

Ability to nimbly adapt
a healthcare system to
evolving evidence

BioVU, the Vanderbilt DNA bank

A clinical laboratory for genomics and pharmacogenomics, linking DNA samples to de-identified electronic medical records





Search

Results

 Search Criteria Find

ICD Codes

- ▶ 001-139 Infectious and parasitic di...
- ▶ 140-239 Neoplasms
- ▶ 240-279 Endocrine, nutritional and
- ▶ 280-289 Diseases of the blood and
- ▶ 290-319 Mental disorders
- ▶ 320-359 Diseases of the nervous s...
- ▶ 360-389 Diseases of the sense org...
- ▶ 390-459 Diseases of the circulatory
- ▶ 460-519 Diseases of the respirator...
- ▶ 520-579 Diseases of the digestive
- ▶ 580-629 Diseases of the genitourin...
- ▶ 630-676 Complications of pregnan...
- ▶ 680-709 Diseases of the skin and ...
- ▶ 710-739 Diseases of the musculos...

Documents

Labs

Vitals

Medications

CPT Codes

Demographics

Local Registries

Genotyping

Include records where:

Group Count: 0

Result Set Total:

0

BioVU Samples Filter:

- None
- Include All BioVU Samples
- Include Non-Compromised Samples

Some BioVU samples can be compromised due to disease related changes in the blood. Genotyping results may be affected.

Shippable Samples:

Include only samples available for external assays

Some BioVU samples cannot be tested outside of Vanderbilt.



Search

Results

Include records where:

▶ ICD Codes

▶ CPT Codes

▼ Labs

▼ PTH/Bone

25DRIA - VITAMIN D 25-OH (RI

DHU - _VITAMIN D 1_25-OH_

H-12D - _VITAMIN D 1_25-OH_

VD25 - VITAMIN D 25-OH

VitD1 - 25 OH VITAMIN D

▶ Nutrition

Group Count: 0

Result Set Total:

0

BioVU Samples Filter:

- None
 Include All BioVU Samples
 Include Non-Compromised Samples

Some BioVU samples can be compromised due to disease related changes in the blood. Genotyping results may be affected.

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Search

Results

Search Criteria Find

vitamin D

Find term in Cri

▶ ICD Codes

▶ CPT Codes

▼ Labs

▼ PTH/Bone

25DR1A - VITAMIN D 25-OH (RI

DHUD - _VITAMIN D 1_25-OH_

H-12D - _VITAMIN D 1_25-OH_

VD25 - VITAMIN D 25-OH

VitD1 - 25 OH VITAMIN D

▶ Nutrition

Lab Criteria

Lab: VD25

Normal Range

- Within Normal Range
- Outside of Normal Range
- Any Value - Lab Exists

Specified Range

- Equals
- Greater Than
- Greater Than or Equal To
- Less Than
- Less Than or Equal To
- Between

Add to Criteria

Cancel

[Help](#) [Feedback](#) - [Contact Us](#) [Logout](#)

Result Set Total:

0

BioVU Samples Filter:

- None
- Include All BioVU Samples
- Include Non-Compromised Samples

Some BioVU samples can be compromised due to disease related changes in the blood. Genotyping results may be affected.

Shippable Samples:

Include only samples available for external assays

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Search Results

Search Criteria Find

Add Group

Save Query

▶ ICD Codes

▶ CPT Codes

▼ Labs

▼ PTH/Bone

25DRIA - VITAMIN D 25-OH (RI

DHUD - _VITAMIN D 1_25-OH_

H-12D - _VITAMIN D 1_25-OH_

VD25 - VITAMIN D 25-OH

VitD1 - 25 OH VITAMIN D

▶ Nutrition

Include records where:

✘ VD25 is Any Value - Lab Exists 13847

✘
 Remove
 Group

⊘
 Exclude
 Group

Group Count: 13847

Result Set Total:
13850
BioVU Samples Filter:

- None
 Include All BioVU
 Samples
 Include
 Non-Compromised Samples

Some BioVU samples can be compromised due to disease related changes in the blood. Genotyping results may be affected.

Shippable Samples:

Include only samples available for external assays

Some BioVU samples cannot be tested outside of Vanderbilt.



Search

Results

 Search Criteria Find

Add Group

Save Query

ICD Codes

- ▶ 001-139 Infectious and parasitic diseases
- ▶ 140-239 Neoplasms
- ▶ 240-279 Endocrine, nutritional and metabolic diseases
- ▶ 280-289 Diseases of the blood and blood-forming organs
- ▶ 290-319 Mental disorders
- ▶ 320-359 Diseases of the nervous system
- ▶ 360-389 Diseases of the sense organs and speech
- ▶ 390-459 Diseases of the circulatory system
- ▶ 460-519 Diseases of the respiratory system
- ▶ 520-579 Diseases of the digestive system
- ▶ 580-629 Diseases of the genitourinary system
- ▶ 630-676 Complications of pregnancy, childbirth and the puerperium
- ▶ 680-709 Diseases of the skin and subcutaneous tissue
- ▶ 710-739 Diseases of the musculoskeletal system

Documents

Labs

Vitals

Medications

CPT Codes

Demographics

Local Registries

Genotyping

Include records where:

✘ VD25 is Any Value - Lab Exists 5497

✘
 Remove Group

⊘
 Exclude Group

Group Count: 5497

Result Set Total:
5500
BioVU Samples Filter:

- None
 Include All BioVU Samples
 Include Non-Compromised Samples

Some BioVU samples can be compromised due to disease related changes in the blood. Genotyping results may be affected.

Shippable Samples:

- Include only samples available for external assays
 Some BioVU samples cannot be tested outside of Vanderbilt.



Search Results

Search Criteria Find

Add Group

Save Query

ICD Codes

Documents

Labs

Vitals

Medications

CPT Codes

Demographics

Local Registries

Genotyping

▼ GWAS

Illumina 660W

Illumina 1M

Illumina OMNI-Quad

Illumina OmniExpress 1.0

HumanOmni5-Quad

▶ Platforms

▶ Targeted

Include records where:

✘ VD25 is Any Value - Lab Exists 5497

 ✘
Remove Group

Group Count: 5497

AND Include records where:

✘ Genotyping for Illumina 660W 3033

✘ OR Genotyping for Illumina 1M 1440

 ✘ OR Genotyping for Illumina
OMNI-Quad 5824

 ✘
Remove Group

 ✘
Exclude Group

Group Count: 10232

Result Set Total:
1075
BioVU Samples Filter:

- None
 Include All BioVU Samples
 Include Non-Compromised Samples

Some BioVU samples can be compromised due to disease related changes in the blood. Genotyping results may be affected.

Shippable Samples:

Include only samples available for external assays
 Some BioVU samples cannot be tested outside of Vanderbilt.

Examples of studies in BioVU

- Searching for genomic variants associated with:
 - Physiologic traits
 - Disease
 - Drug responses
- Searching for phenomic variants associated with
 - DNA polymorphisms (PheWAS)

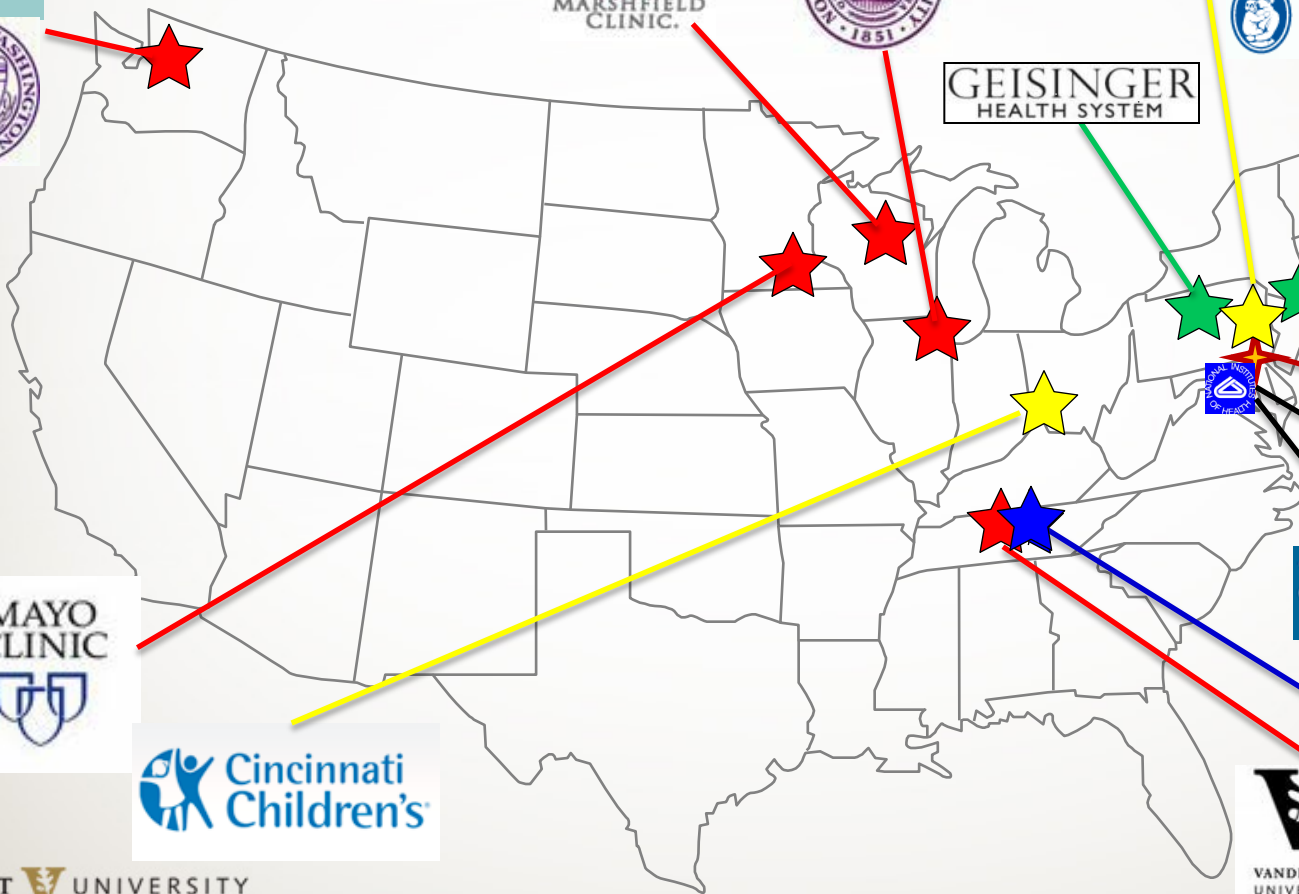
The eMERGE Network

electronic Medical Records & Genomics

A consortium of biorepositories linked to electronic medical records data for conducting genomic studies



Coordinating Center



What is the Phenotype KnowledgeBase?




The reuse of data from electronic medical records (EMRs) and other clinical data systems holds tremendous promise for improving the efficiency and effectiveness of health research. Clinical data in the EMR is a potential source of rich longitudinal data for research, and the recent government efforts to promote the use of EMRs in the clinical setting may further promote the use of such systems in the US healthcare system. As the use of EMRs expands, the demand for usable data from these systems for research has also expanded.




One such effort by the Electronic Medical Records and Genomics Network (eMERGE) has investigated whether data captured through routine clinical care using EMRs can identify disease phenotypes with sufficient positive and negative predictive values for use in genome-wide association studies (GWAS). Most EMRs captured key information (diagnoses, medications, laboratory tests) used to define phenotypes in a structured format; in addition, natural language processing has also been shown to improve case identification rates.*

PheKB is an outgrowth of that validation effort and provides a collaborative environment of building and

Most Recent Phenotypes

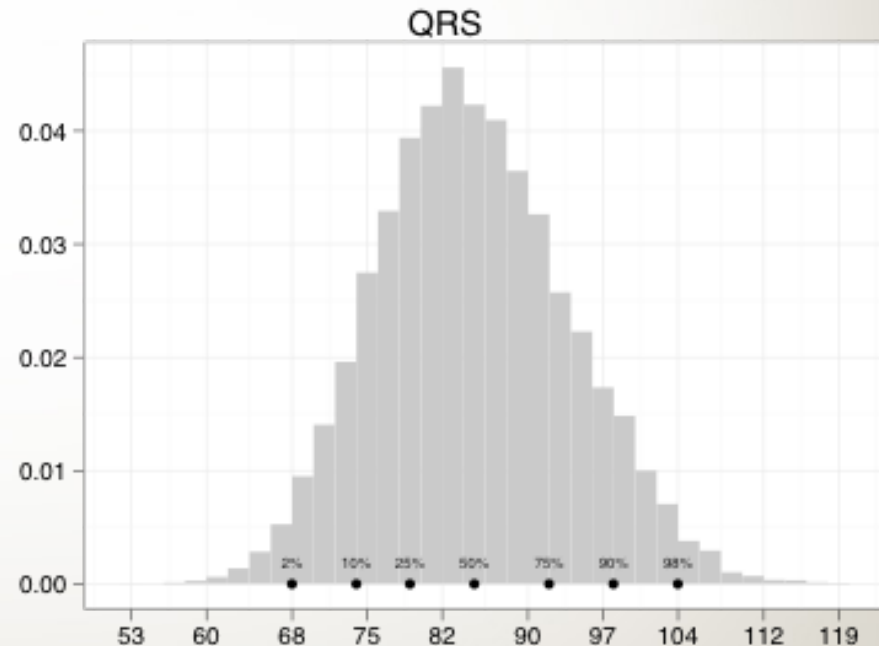
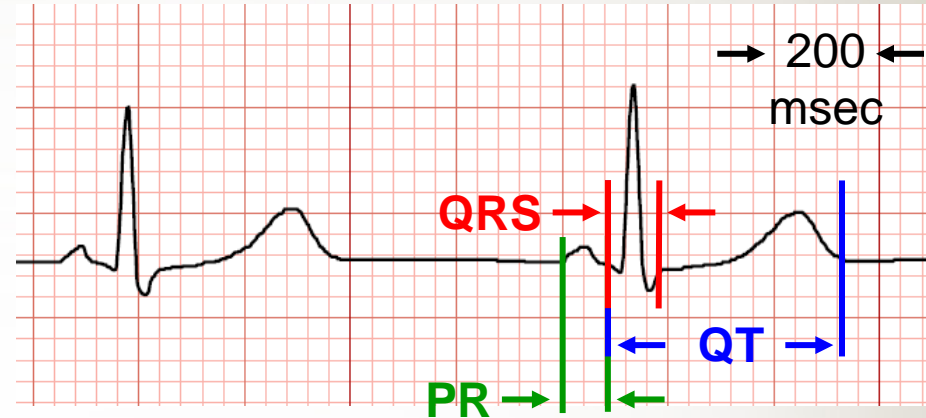
-  Clopidogrel Poor Metabolizers
-  Atrial Fibrillation - Demonstration Project
-  Rheumatoid Arthritis - Demonstration Project
-  Multiple Sclerosis - Demonstration Project
-  Crohn's Disease - Demonstration Project

Title	Groups	Institutions	Data and Methods
 Atrial Fibrillation - Demonstration Project	Demonstration Project	Vanderbilt University	CPT Codes, ICD 9 Codes, Natural Language Processing
 Cardiac Conduction (QRS)	eMERGE Phenotype WG	Vanderbilt University	CPT Codes, ICD 9 Codes, Laboratories, Medications, Natural Language Processing
 Cataracts	eMERGE Phenotype WG	Marshfield Clinic Research Foundation	CPT Codes, ICD 9 Codes, Medications, Natural Language Processing
 Clopidogrel Poor Metabolizers	Denny's Group at Vandy, VESPA - Vanderbilt Electronic Systems for Pharmacogenomic Assessment		CPT Codes, ICD 9 Codes, Laboratories, Medications, Natural Language Processing
 Crohn's Disease - Demonstration Project	Demonstration Project	Vanderbilt University	ICD 9 Codes, Medications, Natural Language Processing
 Dementia	eMERGE Phenotype WG	Group Health Cooperative	ICD 9 Codes, Medications
 Diabetic Retinopathy	eMERGE Phenotype WG	Marshfield Clinic Research Foundation	CPT Codes, ICD 9 Codes, Medications, Natural Language Processing
 Height	eMERGE Phenotype WG	Northwestern University	ICD 9 Codes, Laboratories, Medications
 High-Density Lipoproteins (HDL)	eMERGE Phenotype WG	Marshfield Clinic Research Foundation	ICD 9 Codes, Laboratories, Medications, Natural Language Processing
 Hypothyroidism	eMERGE Phenotype WG	Vanderbilt University	CPT Codes, ICD 9 Codes, Laboratories, Medications, Natural Language Processing
 Lipids	eMERGE Phenotype WG	Northwestern University	ICD 9 Codes, Laboratories, Medications
 Multiple Sclerosis - Demonstration Project	Demonstration Project	Vanderbilt University	ICD 9 Codes, Medications, Natural Language Processing
 Peripheral Arterial Disease	eMERGE Phenotype WG	Mayo Clinic	CPT Codes, ICD 9 Codes, Laboratories, Medications, Natural Language Processing
 Red Blood Cell Indices	eMERGE Phenotype WG	Mayo Clinic	CPT Codes, ICD 9 Codes, Laboratories, Medications, Natural Language Processing

-  Multiple Sclerosis - Demonstration Project
-  Crohn's Disease - Demonstration Project
-  Atrial Fibrillation - Demonstration Project

QRS duration in the normal ECG

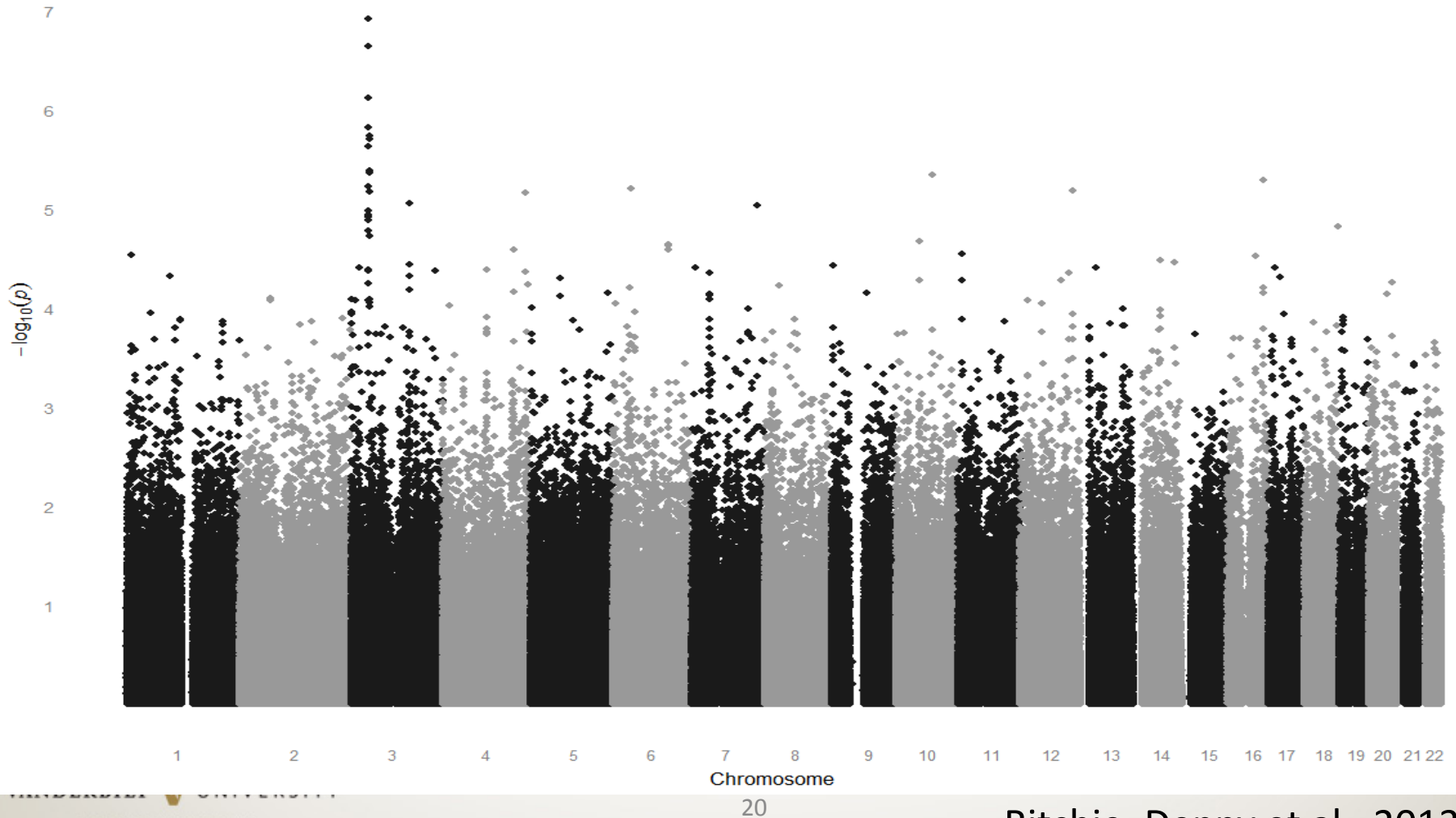
- QRS duration is an index of conduction velocity in heart. Longer QRS implies slow conduction. Slow conduction predisposes to arrhythmias.
- Algorithms developed to identify records in which the 1st ECG is normal and
 - no heart disease
 - normal electrolytes
 - no confounding drugs
- Deployed in the entire electronic record → 30,363



GWAS of QRS Duration

SCN5A/SCN10A

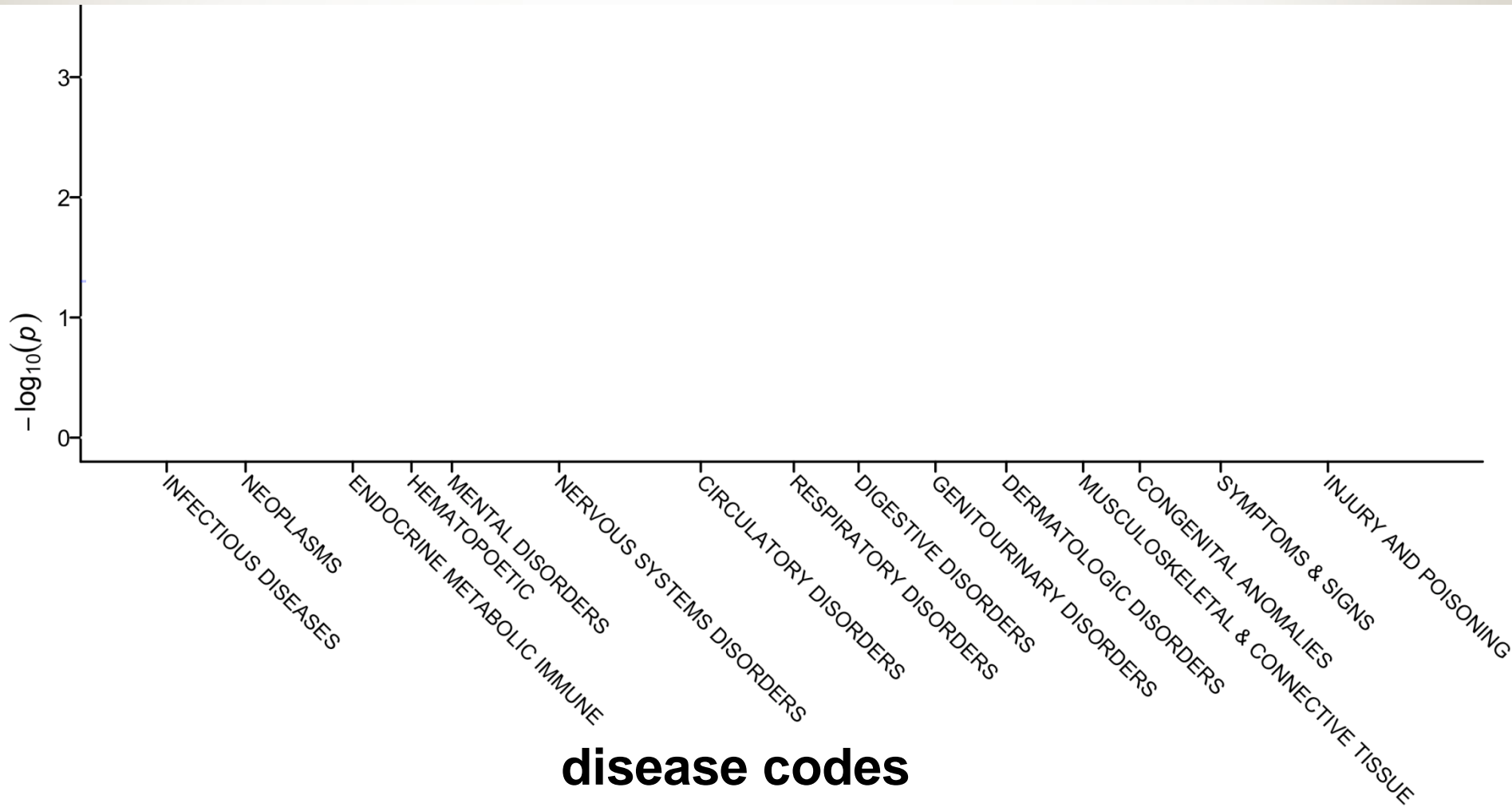
n=5,272



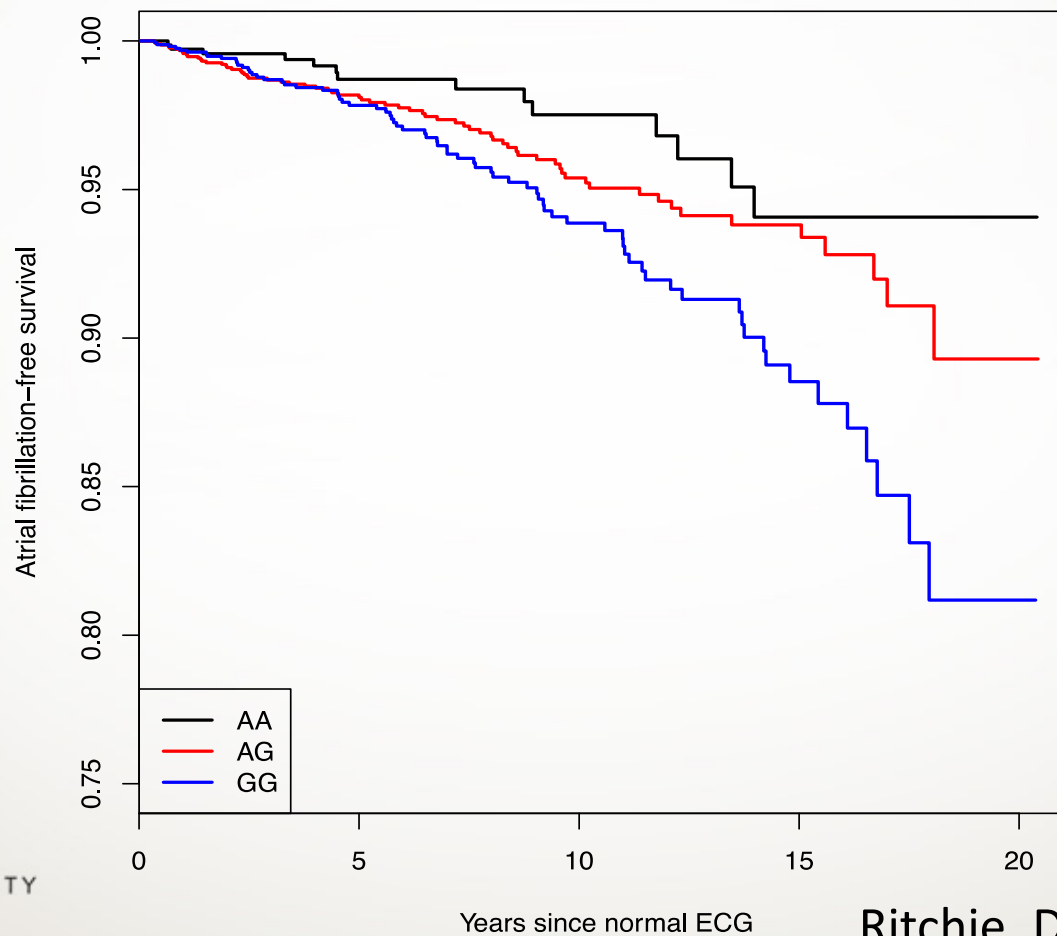
Ritchie, Denny et al., 2013

Φ WAS

PHEnome Wide Association Study

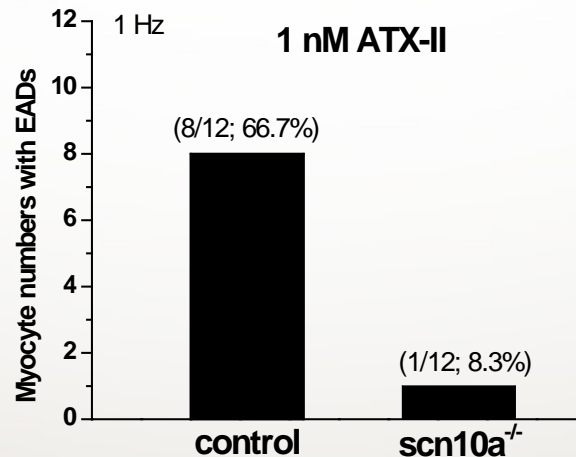
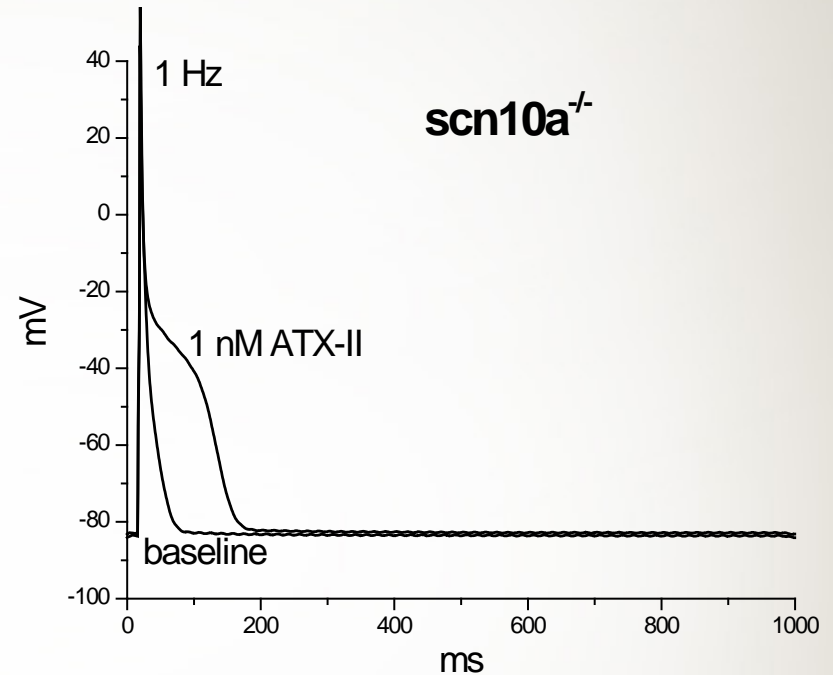
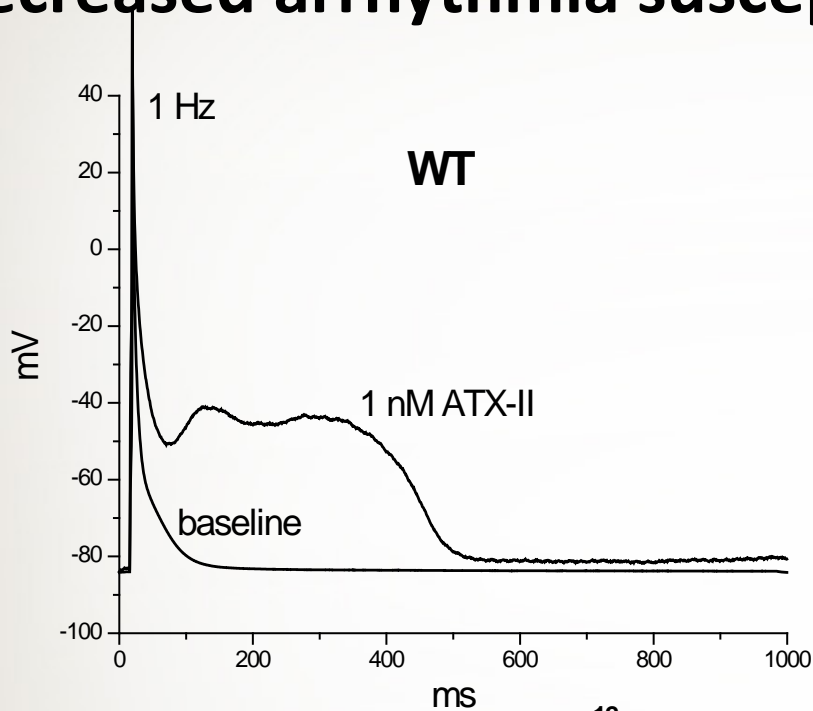


rs6795970 (SCN10A) is associated not only with variability in normal QRS but also with development of atrial fibrillation

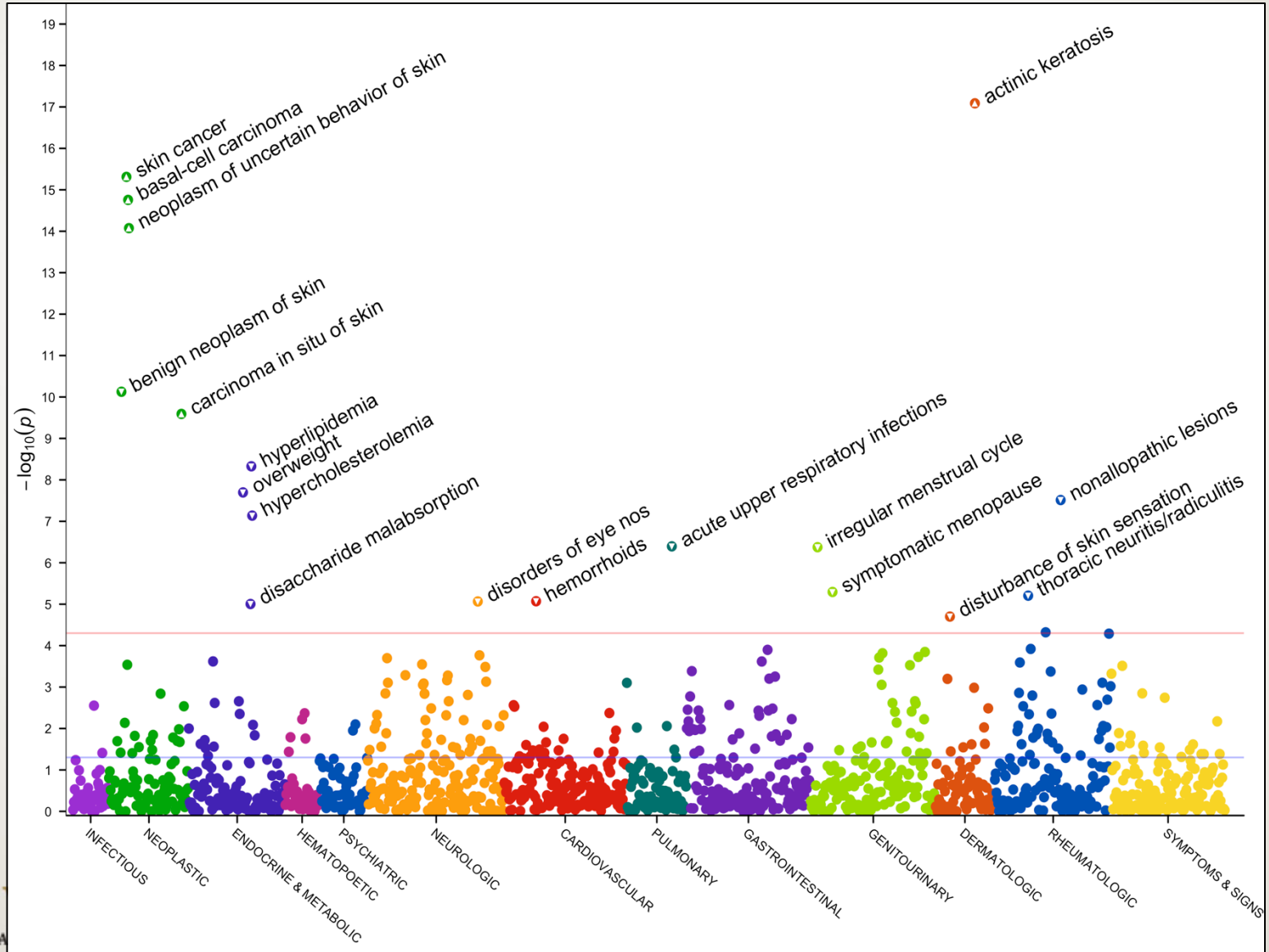


A not irrelevant digression...

Decreased arrhythmia susceptibility in *scn10a*^{-/-} myocytes



Pleiotropy: PheWAS associations with a skin color SNP



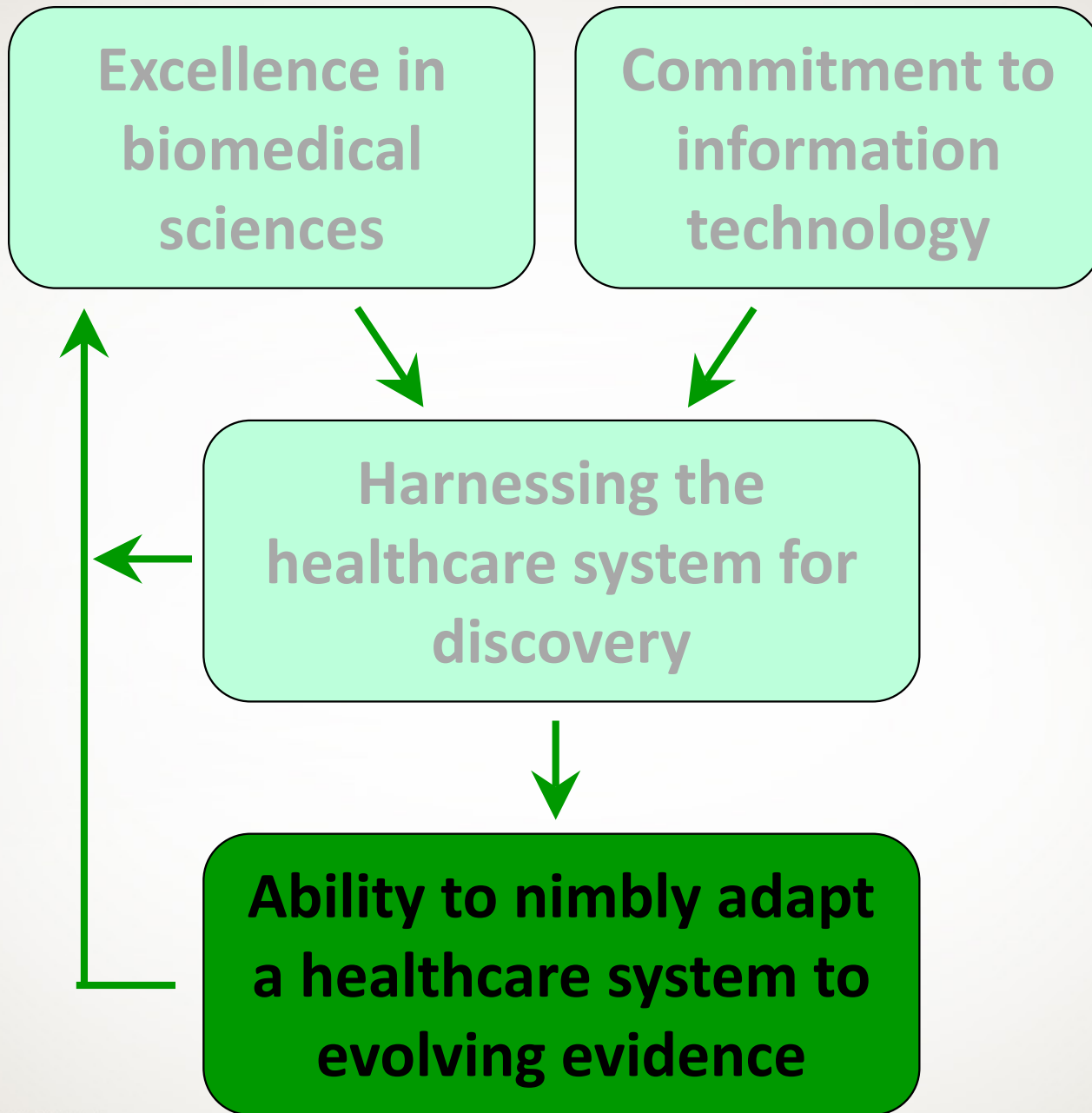
EMR-linked biobanks in eMERGE-II

Site	Participants	(GWAS)- Genotyped Samples
------	--------------	---------------------------------

A paradox

Large numbers of patients, of diverse ancestries, are required to develop evidence to “personalize” medicine.

Mt. Sinai	22,000	2,867
CHOP	60,000	22,000
Cincinnati/Boston	10,000	3,000
TOTAL	328,895	75,983





Pharmacogenomics Research Network

U.S. Department of Health & Human Services

FDA U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

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SEARCH

Most Popular Searches

Home | Food | Drugs | Medical Devices | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Radiation-Emitting Products | Tobacco Products

Drugs

Home > Drugs > Science & Research (Drugs) > Additional Research Areas

- Science & Research (Drugs)
- Additional Research Areas
- Genomics
- Overview of the Genomics Group
- Presentations on Genomics
- Publications on Genomics

Table of Pharmacogenomic Biomarkers in Drug Labels

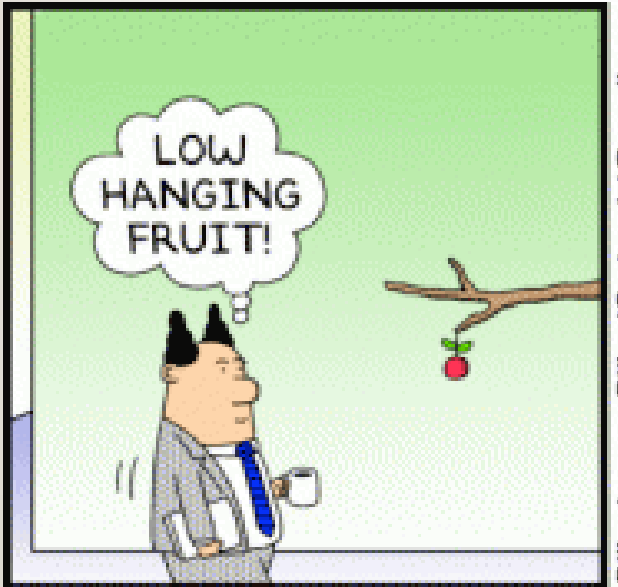
Pharmacogenomics can play an important role in identifying responders and non-responders to medications, avoiding adverse events, and optimizing drug dose. Drug labels may contain information on genomic biomarkers and can describe:

- Drug exposure and clinical response variability
- Risk for adverse events
- Genotype-specific dosing
- Mechanisms of drug action
- Polymorphic drug target and disposition genes

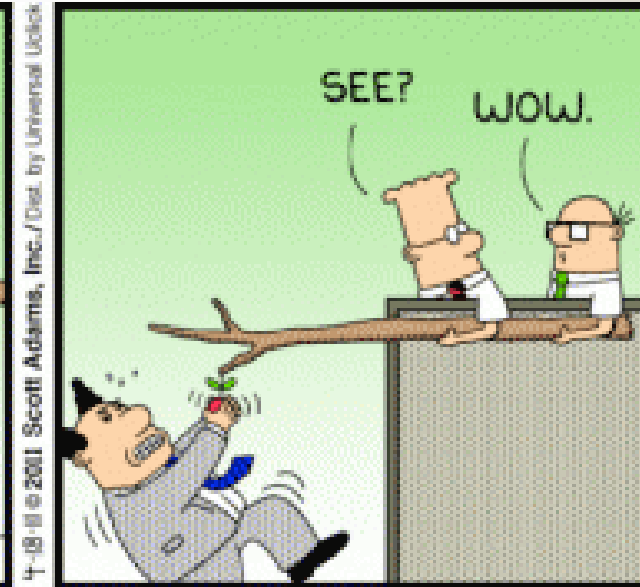
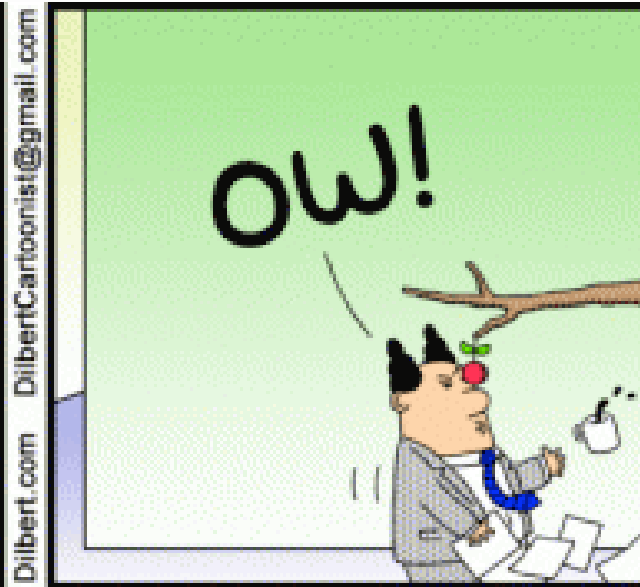
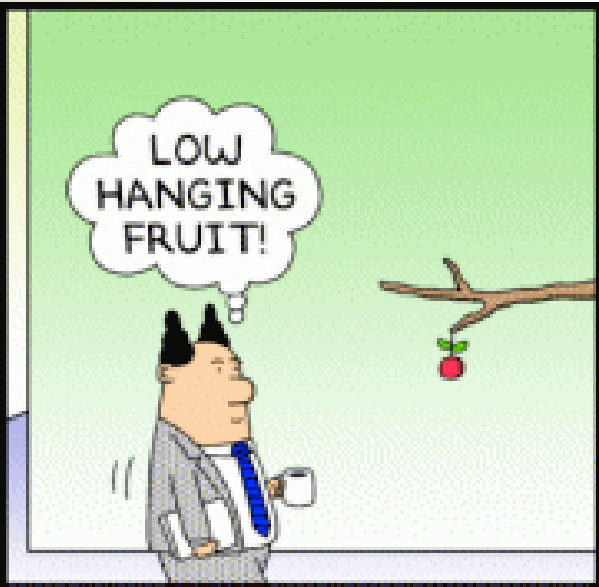
The table below lists **FDA-approved drugs with pharmacogenomic information in their labels**. Some, but not all, of the labels include specific actions to be taken based on genetic information. Relevant sections of the

n=58 (germline)

Pharmacogenomics: even low hanging fruit...



...is not so simple

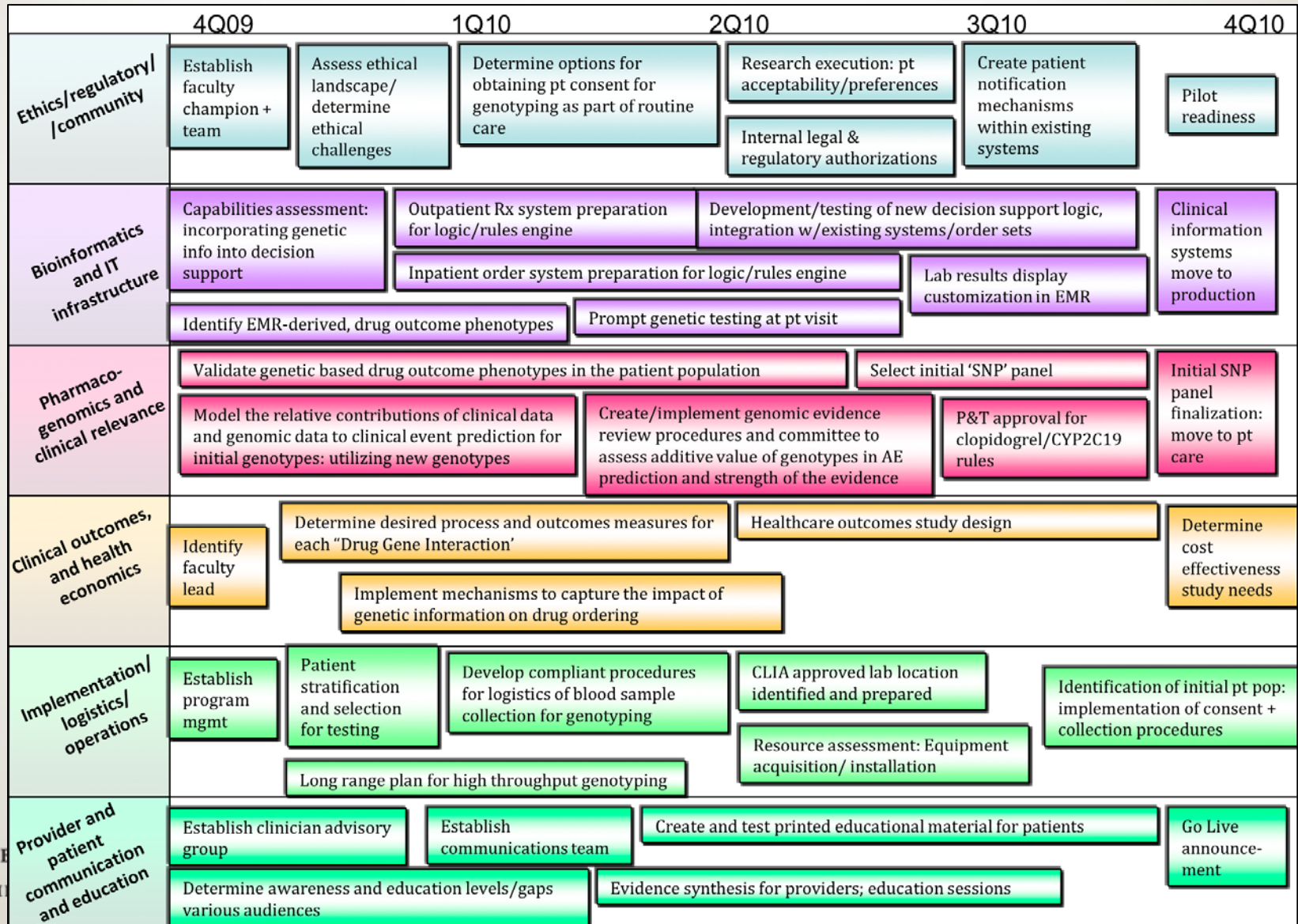


Dilbert.com DilbertCartoonist@gmail.com

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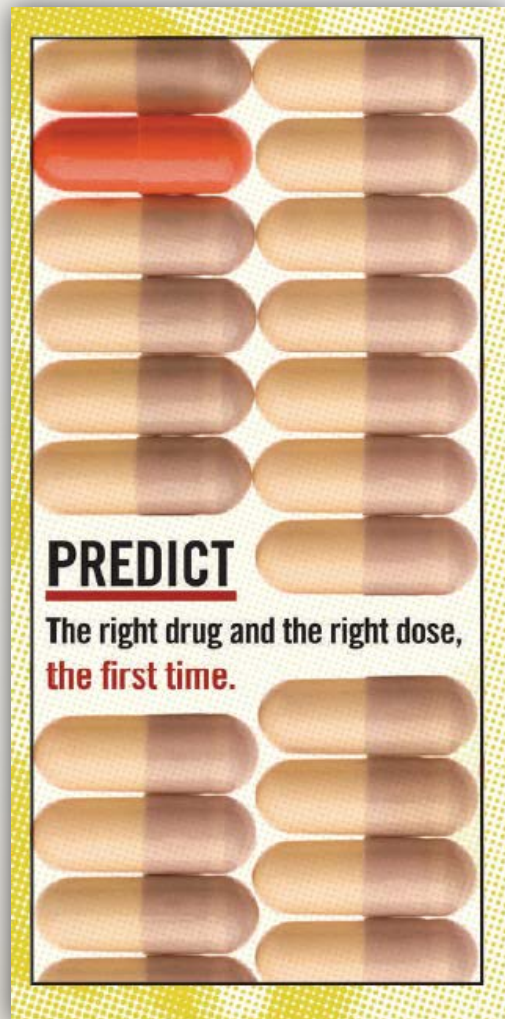
Planning the PREDICT Project

Pharmacogenomic Resource for Enhanced Decisions In Care and Treatment



PREDICT

Pharmacogenomic Resource for Enhanced Decisions In Care and Treatment

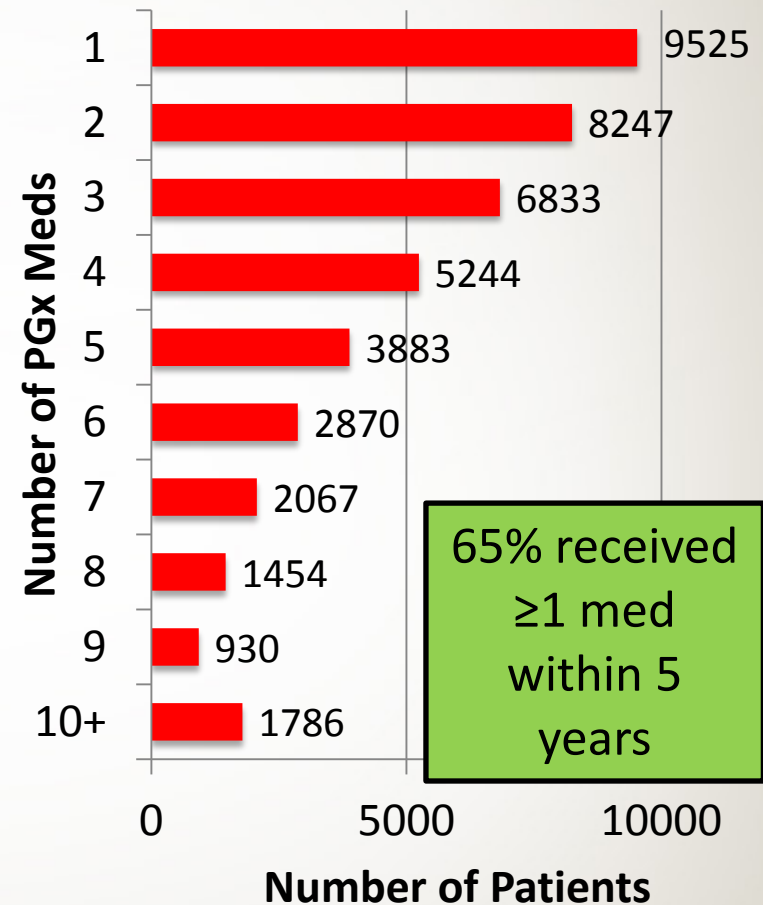


1. Select populations of patients who are “**at high risk**” for receiving a drug with an actionable “pharmacogenetic” story.
2. Genotype all of them on a platform that assays genotypes important for variable actions of many drugs preemptively.
3. Store the genotypes, develop the informatics tools to provide point-of-care advice. Track outcomes. **The “easy stuff”**.

Who is at “high risk”?

A case for preemptive genotyping

In a cohort of 53,196 “Medical Home” patients followed for up to 5 years, how many received drug(s) that have a recognized pharmacogenetic “story”?




Clopidogrel label revision March 2010 identifies another **high risk** group

WARNING: DIMINISHED EFFECTIVENESS IN POOR METABOLIZERS

...ation for complete boxed warning.

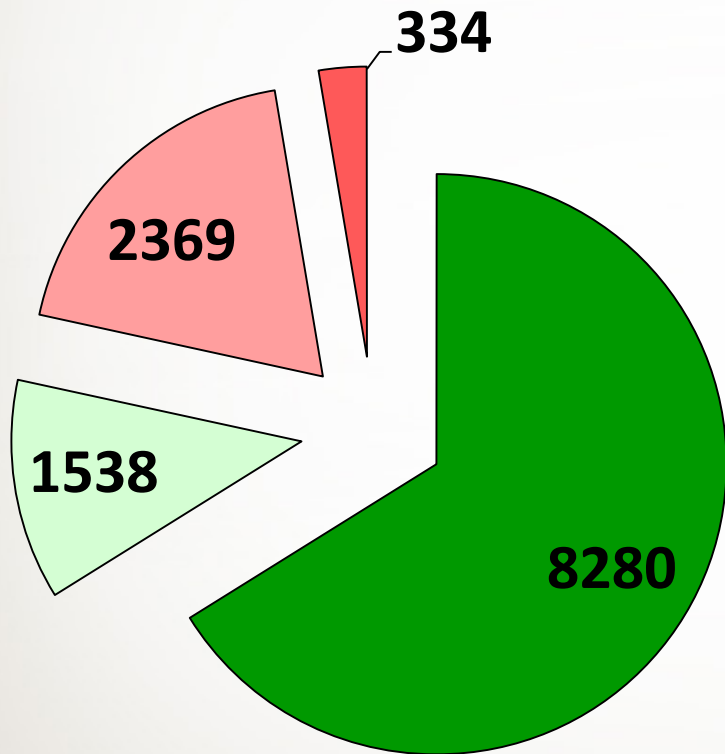
- Effe... ds on activation to an active metabolite by the CYP2C19 system, principally **CYP2C19**. (5.1)
- Poor... h Plavix at recommended doses exhibit high... rates following acute coronary syndrome (ACS) primary intervention (PCI) than patients with normal... (2.5)
- Test... a patient's CYP2C19 genotype and can be used to guide therapeutic strategy. (12.5)
- Consider alternative treatment or treatment strategies in patients identified as CYP2C19 poor metabolizers. (2.3, 5.1)



In BioVU: Vascular events during clopidogrel (205 cases; 493 controls)

SNP (Gene)	Genotype	Odds Ratio (vs *1/*1)	P
rs4244285 (CYP2C19*2)	*1/*2 or *2/*2	1.54	0.003
rs1045642 (ABCB1)	3435 C→T	1.28	0.018

CYP2C19 genotypes in 12,521 PREDICT patients (9/2010-4/2013)



2.7% homozygous
18.9% heterozygous
12.2% non-actionable variant
66.1% no common variant



Go: [Back](#) | [Workbook](#)

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[-genetic Risks](#) [Cross-DGI Risk](#) [PREDICT Website](#) [Metadata](#) [Requirements Documentation](#) [Gene R](#)

DGI	Gene Effect	Gene Result	Number of Patients	% of Total Patients
clopidogrel CYP2C19	hypo metabolizer	(*3 VAR)	2	0.60%
		(*8 VAR)	1	0.30%
		*2 HET;(*6 HET)	1	0.30%
		*2 HET;*3 HET	6	1.80%
		*2 HET;*4 HET	9	2.69%
		*2 HET;*8 HET	8	2.40%
		*2 VAR	306	91.62%
		*3 HET;*4 HET	1	0.30%
		Total	334	100.00%
		intermediate metabolizer		(*6 HET)
*2 HET	2,284			96.41%
*3 HET	10			0.42%
*4 HET	33			1.39%
*6 No Call;*8 HET	1			0.04%
*8 HET	38			1.60%
Total	2,369			100.00%
Total		2,703	100.00%	
Grand Total		2,703	100.00%	

Point of care decision support

HEO Popup - [Order Entry]



Clopidogrel Poor Metabolizer Rules

Genetic testing has been performed and indicates this patient may be at risk for inadequate anti-platelet response to clopidogrel (Plavix®) therapy

This patient has been tested for CYP2C19 variants, and has identified the presence of two copies of a risk allele which is associated with poor metabolism of clopidogrel. Poor metabolizers treated with clopidogrel at normal doses exhibit higher rates of stent thrombosis/other cardiovascular events.

(See StarPanel for patient-specific CYP2C19 gene result.)

Treatment modification is recommended if not otherwise contraindicated:

Click here for [more information](#)

- Prescribe prasugrel (EFFIENT) **60 mg** x 1 dose now, followed by 10mg daily to start at 10am tomorrow
- Prescribe ticagrelor (BRILINTA) **180 mg** x1 dose now, followed by 90 mg twice daily to start at 10am tomorrow

If prasugrel (EFFIENT) or ticagrelor (BRILINTA) are not selected, please choose desired action:

Click here for [more information](#)

- Maintain requested daily dose of clopidogrel (PLAVIX)

75 mg Daily, start

Select medication route:

Order

Cancel

NOTE: The Vanderbilt P&T Committee recommends that prasugrel or ticagrelor replace clopidogrel for poor metabolizers unless contradicted, if feasible. If this is not possible maintain standard dose of clopidogrel. The guidelines above were developed based on outcome studies of patients who received a stent into a coronary artery.

Back

Home

Close

Personalizing medicine



Variability is the law of life, and as no two faces are the same, so no two bodies are alike, and no two individuals react alike and behave alike under the abnormal conditions which we know as disease.

Sir William Osler

Firefox

StarPanel - Roden, Dan M. (rod...)

User rodewui (Roden, Dan M.) docs4u results4u: 60 SignDrafts Messages:1 (RodenD-MD) Unsaved Work: 1

Pt.Chart ADVANCE StNotes Forms OPOC Quill Rx ProvCom Panels Pt.Lists TaskList MsgBskts WhBoards NewRes SignDrafts Misc.

code status: No Data Alert PCP: [REDACTED]

AllDocuments Apptm. Calend. EnterData Faxed Flows FastLabs Labs Meds Msgs? Reminders? Orders Pt.summary Search AddToPanel

VitalSigns DCINoDoc

CancerStage ClinicIntake Disclosure Forms Favorites Immuniz. NewMsg Pt.Letter Provider.Letter Provider.Comm.Wizard ReferralMsg

General Information: (12/05/12 09:05, Teresa
[REDACTED]
PCP: [REDACTED]
Card: [REDACTED]
Arrhythmia/Device: Dr. Dan Roden, VUMC

Structured Problems: (12/05/12 09:05, Teresa
[REDACTED]

- Coronary artery disease [.]
- Aortic valve stenosis [-severe]
- Congestive heart failure [.]
- Mitral valve regurgitation [.]
- Chronic atrial fibrillation [.]
- Hypertension [.]
- Hyperlipidemia [.]
- Gastroesophageal reflux disease [.]
- 9. Chronic Renal insufficiency
- Paroxysmal ventricular tachycardia s/p VTach cardiac arrest, 6/12/09
- ICD Shock for VTach, 9/14/2010
- Hx Blood Transfusion:
- Anesthesia Difficulties:
- Dental Hygiene:
- Emergent #:

Significant Procedures: (12/05/12 09:05, Teresa

Adverse and Allergic Drug Reactions: (02/21/13 12:25, [REDACTED]
[REDACTED]
Aldactone (rash)

Drug Genome Interactions: (01/05/12 13:03)
clopidogrel sensitivity: NORMAL METABOLIZER - gene: CYP2C19 - gene result: *1/*1
warfarin sensitivity: Hyper Responder - gene results: VKORC1 G/G; CYP2C9 *1/*3
simvastatin sensitivity: HIGH MYOPATHY RISK, MINOR ALLELE HOMOZYGOUS (C;C) - gene: SLCO1B1 - gene result: *5/*5
thiopurine sensitivity: INTERMEDIATE MYELOTOXICITY RISK, MINOR ALLELE HETEROZYGOUS - gene: TPMT - gene result: *1/*3c
tacrolimus sensitivity: HYPO RESPONDER - gene: CYP3A5 - gene result: *1/*3
Note: Most genetic variants with therapeutic considerations demonstrate reproducibility of greater than 98%. Please visit www.mydruggenome.org for additional information.

Medications: [prepare to print](#) [print and give pt.](#) [Show Hx of medications](#) [Drug/Herb Interactions](#) (02/21/13 12:25, [REDACTED]
[REDACTED]

- Simvastatin (zocor) 20 mg orally nightly
- Quinapril (accupril) 40 mg orally daily
- Zolpidem (ambien) 10mg orally daily
- Carvedilol (coreg) 6.5 mg orally twice daily with meals
- Furosemide (lasix) 20 mg 3 tablets orally daily
- Digoxin (lanoxin) 0.125 mg 1/2 tablet orally daily
- Warfarin (coumadin) 2 mg, 2 tablets on sun by mouth and 1 1/2 tablet on other days**
- Potassium (k-dur) 10meq 3 tablets orally daily

EBM resources

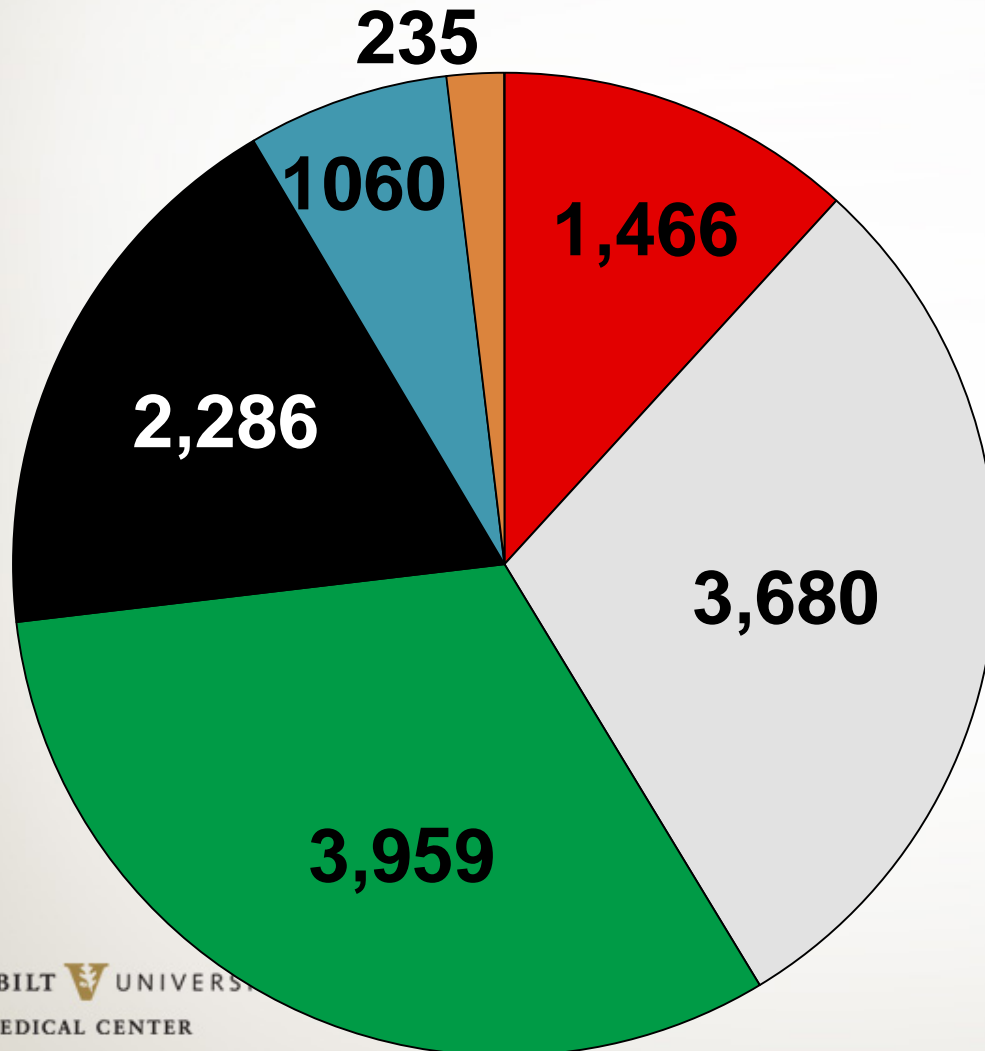
Displaying SNaPshot results for mutation-specific therapy in melanoma in the EMR

MR#	Patient Name	Actions	Tumor Gene Mutations							
			H-SMP	BRAF	CTNNB1	GNAT1	GNAQ	KIT	NRAS	
03	81	A, B M.	Actions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
03	56	A, P	Actions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
03	35	B, J A	Actions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
01	80	B, S A	Actions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
02	29	E, J E	Actions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
02	27	F, R M	Actions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
02	77	G, T	Actions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
02	73	H, A	Actions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
03	64	S, C	Actions	A						
02	79	S, A S	Actions	R						
02	40	W, J E I	Actions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
03	74	W, C L	Actions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

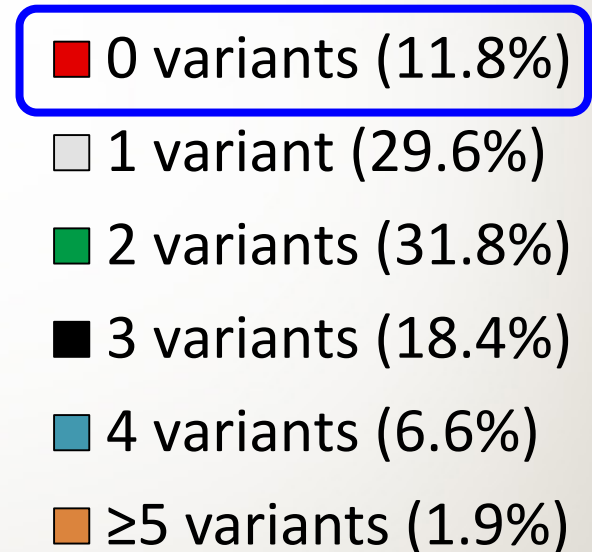
BRAF c.1798_1799GT>AG (V600R) Not Detected
 BRAF c.1798_1799GT>AA (V600K) Not Detected
BRAF c.1799T>A (V600E) Detected
 BRAF c.1799_1800TG>AA (V600E) Not Detected
 BRAF c.1798G>A (V600M) Not Detected
 BRAF c.1799T>G (V600G) Not Detected
 BRAF c.1799_1800TG>AT (V600D) Not Detected

Multiplexed testing for pharmacogenetic variants

(after 5 drug-gene pairs...)



Total n=12,451
(9/10-4/13)



Engaging patients

The screenshot shows a web browser window displaying the 'My Health at Vanderbilt' patient portal. The browser's address bar shows the URL 'https://www.myhealthatvanderbilt.com/'. The page header includes the Vanderbilt University Medical Center logo and navigation links for 'Community events', 'Pay JANE DOE's Bill', and 'Hi, JANE DOE'. The main content area is titled 'My Health at Vanderbilt' and features a 'MY TOOLS' section with six interactive tiles: 'My Record' (highlighted with a green dashed border), 'My Forms', 'Messages', 'Health Management', 'Appointments', and 'My Account'. Each tile includes an icon and a brief description of the service. On the right side, there is a video player titled 'Our Promise to You Watch video' showing a doctor and a patient. At the bottom, there are links for 'All Health Topics' and 'Health News You Can Use', with a snippet of an article about the 'Vanderbilt's BioVU Databank'.

https://www.myhealthatvanderbilt.com/

My Health At Vanderbilt | Testing Volume by Provider | StarPanel

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VANDERBILT UNIVERSITY MEDICAL CENTER | Community events | Pay JANE DOE's Bill | Hi, JANE DOE

My Health at Vanderbilt

MY TOOLS

- My Record**
See lab results, vaccine records and more.
- My Forms**
View forms you use when visiting your health provider.
- Messages**
Contact your provider's office. You have
- Health Management**
Set health goals and track your progress.
- Appointments**
Request or view an appointment.
- My Account**
View your settings, invite delegates and more.

Our Promise to You
Watch video

All Health Topics
Read about health topics specific to you

Health News You Can Use
Vanderbilt's BioVU Databank Now World's Largest Human DNA Repository Linked to Searchable, Electronic Health Information

Engaging patients

The screenshot shows a web browser window displaying the My Health At Vanderbilt patient portal. The browser's address bar shows the URL <https://www.myhealthatvanderbilt.com/>. The page header includes the Vanderbilt University Medical Center logo, navigation links for "Community events", "Pay JANE DOE's Bill", and a user greeting "Hi, JANE DOE". A main navigation bar contains icons for "My Record", "Messages", "Appointments", "My Forms", "Health Management", and "My Account". Below this, a "View My Clinical Record" button is visible, with a sub-button "Genes that Affect My Medicines" highlighted by a green dashed border. To the right, there is a video player titled "Our Promise to You Watch video" featuring a doctor and a patient. The footer contains contact information for the Vanderbilt University Medical Center, including the address "1211 Medical Center Drive, Nashville, TN 37232", the phone number "(615) 936-6963", and the "Vanderbilt Central Appointment Office". The Vanderbilt University logo and name are also present, along with a commitment statement and the version number "8.2.6-prod".

https://www.myhealthatvanderbilt.com/ My Health At Vanderbilt Testing Volume by Provider StarPanel -

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VANDERBILT UNIVERSITY MEDICAL CENTER Community events Pay JANE DOE's Bill Hi, JANE DOE

MY HEALTH HOME HELP

GUIDE For Patients and Visitors

My Record Messages Appointments My Forms Health Management My Account

View My Clinical Record

Genes that Affect My Medicines

Our Promise to You Watch video

Vanderbilt University Medical Center • 1211 Medical Center Drive, Nashville, TN 37232 (615) 936-6963 Vanderbilt Central Appointment Office

VANDERBILT UNIVERSITY MEDICAL CENTER

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Engaging patients

The screenshot shows a patient portal interface. At the top, there is a navigation bar with six items: My Record (highlighted in orange), Messages, Appointments, My Forms, Health Management, and My Account. Below the navigation bar is a section titled "Personalized Medicine". A paragraph explains that each person responds differently to medicines and that genetic tests can help predict and prevent bad drug side effects. Below this is a table with two columns: "Medication" and "Does your genetic test result affect your response to medicines?". The table lists five medications: Clopidogrel/Plavix (Yes), Simvastatin/Zocor (Yes), Tacrolimus (No), Thiopurine Therapy (No), and Warfarin/Coumadin (Yes). To the right of the table, there are two sections: "The Clopidogrel Test" with a "Show less >" link, and "Your Risk" with a "Show less >" link. On the left side of the portal, there is a sidebar with a logo, "MY HEALTH HOME", "HELP", and "GUIDE For Patients and Visitors".

Medication	Does your genetic test result affect your response to medicines?
Clopidogrel/Plavix [®]	Yes
Simvastatin/Zocor [®]	Yes
Tacrolimus [®]	No
Thiopurine Therapy [®]	No
Warfarin/Coumadin [®]	Yes

The Clopidogrel Test
Show less >

Clopidogrel (sounds like "kloh-PID-oh-grel") is a blood thinner used to prevent clots that can cause a heart attack or stroke. Your genes can affect how well the drug works. This genetic test identifies how well you may respond to clopidogrel.

Your Risk
Show less >

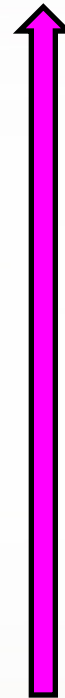
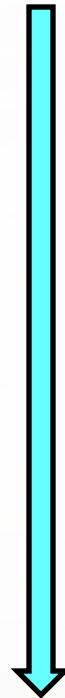
eMERGE-PGRN Partnership



Pharmacogenomics
Research Network

PGx capabilities:

- Array-based assay for pharmacogenes
- Drug-gene guidelines
- CLIA & QC standards



EMR-informatics capabilities

- Privacy
- Electronic phenotyping
- Large populations

The eMERGE Network
electronic Medical Records & Genomics

Lessons (1)

- A key role for discovery
- Even “low-hanging fruit” is complicated:
 - Multiple variant alleles
 - some common
 - some rare and of unknown function
 - some not so simple to genotype
 - Variability by ancestry

Lessons (2)

- Multidisciplinary:

- basic & clinical pharmacology
- genome science
- statistics
- informatics
- ethics
- hospital administration
- clinical pathology
- clinicians
- user interface expertise
- nursing
- pharmacy
- outcomes; economics

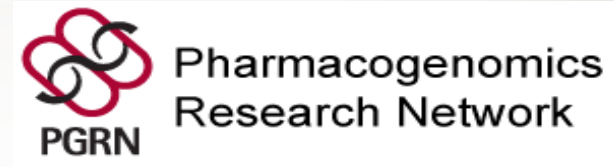
- Engagement:

- Domain expertise/users: each new “pair” requires coupled pharmacogenomic and clinical domain expertise
- Patients
- Need for specific domain physician champions

Lessons (3)

- Educational needs from students to practitioners
- Understanding changing levels of evidence
- Need for extremely high quality genomic data for clinical purposes
- Absolute (?) requirement for advanced electronic medical records to
- Institutional will

The Teams



First data peek...

- 7405 PREDICT genotyped patients from 10/1/2010 to 6/30/2012:
 - 1620 with stent placed
 - “final” antiplatelet therapy identified at 90 days

