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

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.

Francis Collins, NEJM 9/16/2009
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

April 24, 2013

163,941

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Search Criteria

vtamin D

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

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.
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
Search Criteria
- vitamin D
- 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

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

Ramirez et al, 2011
GWAS of QRS Duration

SCN5A/SCN10A

n=5,272

Ritchie, Denny et al., 2013
ΦWAS
PHEnome Wide Association Study

-d_{10}(p)

Disease codes

Ritchie, Denny et al., 2013
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*<sup>-/-</sup> myocytes
Pleiotropy: PheWAS associations with a skin color SNP
A paradox
Large numbers of patients, of diverse ancestries, are required to develop evidence to “personalize” medicine.
Excellence in biomedical sciences

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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
Planning the PREDICT Project

Pharmacogenomic Resource for Enhanced Decisions In Care and Treatment

<table>
<thead>
<tr>
<th></th>
<th>4Q09</th>
<th>1Q10</th>
<th>2Q10</th>
<th>3Q10</th>
<th>4Q10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethics/regulatory/community</td>
<td>Establish faculty champion + team</td>
<td>Assess ethical landscape/ determine ethical challenges</td>
<td>Determine options for obtaining pt consent for genotyping as part of routine care</td>
<td>Research execution: pt acceptability/preferences</td>
<td>Create patient notification mechanisms within existing systems</td>
</tr>
<tr>
<td>Bioinformatics and IT infrastructure</td>
<td>Capabilities assessment: incorporating genetic info into decision support</td>
<td>Outpatient Rx system preparation for logic/rules engine</td>
<td>Development/testing of new decision support logic, integration w/ existing systems/order sets</td>
<td>Inpatient order system preparation for logic/rules engine</td>
<td>Lab results display customization in EMR</td>
</tr>
<tr>
<td>Pharmacogenomics and clinical relevance</td>
<td>Validate genetic based drug outcome phenotypes in the patient population</td>
<td>Identify EMR-derived, drug outcome phenotypes</td>
<td>Prompt genetic testing at pt visit</td>
<td>Select initial ‘SNP’ panel</td>
<td>Clinical information systems move to production</td>
</tr>
<tr>
<td>Clinical outcomes, and health economics</td>
<td>Model the relative contributions of clinical data and genomic data to clinical event prediction for initial genotypes: utilizing new genotypes</td>
<td>Determine desired process and outcomes measures for each “Drug Gene Interaction”</td>
<td>Implement mechanisms to capture the impact of genetic information on drug ordering</td>
<td>Healthcare outcomes study design</td>
<td>Determine cost effectiveness study needs</td>
</tr>
<tr>
<td>Implementation/logistics/operations</td>
<td>Establish program mgmt</td>
<td>Patient stratification and selection for testing</td>
<td>Develop compliant procedures for logistics of blood sample collection for genotyping</td>
<td>CLIA approved lab location identified and prepared</td>
<td>Identification of initial pt pop: implementation of consent + collection procedures</td>
</tr>
<tr>
<td>Provider and patient communication and education</td>
<td>Establish clinician advisory group</td>
<td>Establish communications team</td>
<td>Create and test printed educational material for patients</td>
<td>Go Live announcement</td>
<td></td>
</tr>
</tbody>
</table>

- Assignments are color-coded for clarity.
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”.

PREDICT
Pharmacogenomic Resource for Enhanced Decisions In Care and Treatment
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”? 65% received ≥1 med within 5 years.
Clopidogrel label revision March 2010 identifies another high risk group

<table>
<thead>
<tr>
<th>SNP (Gene)</th>
<th>Genotype</th>
<th>Odds Ratio (vs *1/*1)</th>
<th>P</th>
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<tr>
<td>rs4244285 (CYP2C19*2)</td>
<td>*1/*2 or *2/*2</td>
<td>1.54</td>
<td>0.003</td>
</tr>
<tr>
<td>rs1045642 (ABCB1)</td>
<td>3435 C→T</td>
<td>1.28</td>
<td>0.018</td>
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</tbody>
</table>

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

Delaney et al., 2012
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
<table>
<thead>
<tr>
<th>DGI</th>
<th>Gene Effect</th>
<th>Gene Result</th>
<th>Number of Patients</th>
<th>% of Total Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>clopidogrel</td>
<td>hypo metabolizer</td>
<td>(*3 VAR)</td>
<td>2</td>
<td>0.60%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(*8 VAR)</td>
<td>1</td>
<td>0.30%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*2 HET;(*6 HET)</td>
<td>1</td>
<td>0.30%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*2 HET;*3 HET</td>
<td>6</td>
<td>1.80%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*2 HET;*4 HET</td>
<td>9</td>
<td>2.69%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*2 HET;*8 HET</td>
<td>8</td>
<td>2.40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*2 VAR</td>
<td>306</td>
<td>91.62%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*3 HET;*4 HET</td>
<td>1</td>
<td>0.30%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>334</td>
<td>100.00%</td>
</tr>
<tr>
<td>intermediate</td>
<td>metabolizer</td>
<td>(*6 HET)</td>
<td>3</td>
<td>0.13%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*2 HET</td>
<td>2,284</td>
<td>96.41%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*3 HET</td>
<td>10</td>
<td>0.42%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*4 HET</td>
<td>33</td>
<td>1.39%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*6 No Call;*8 HET</td>
<td>1</td>
<td>0.04%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*8 HET</td>
<td>38</td>
<td>1.60%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>2,369</td>
<td>100.00%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td>2,703</td>
<td>100.00%</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td></td>
<td></td>
<td>2,703</td>
<td>100.00%</td>
</tr>
</tbody>
</table>
Point of care decision support

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 10am

Select medication route: PO

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.
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
General Information: (12/05/12 09:03, Teresa)

PCP: 

Arrhythmia/Device: Dr. Dan Roden, VUMC

Structured Problems: (12/05/12 09:03, Teresa)

- Coronary artery disease
- Aortic valve stenosis
- 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 09:03, Teresa)

Adverse and Allergic Drug Reactions: (02/21/13 12:25)

- 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)

- Simvastatin (zocor) 20 mg orally nightly
- Quinapril (acquapril) 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
Displaying SNaPshot results for mutation-specific therapy in melanoma in the EMR

<table>
<thead>
<tr>
<th>MR#</th>
<th>Patient Name</th>
<th>Actions</th>
<th>Tumor Gene Mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>03</td>
<td>81 A, B M.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>03</td>
<td>56 A, P</td>
<td></td>
<td></td>
</tr>
<tr>
<td>03</td>
<td>35 B, J A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>01</td>
<td>80 B, S A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>02</td>
<td>29 E, J E</td>
<td></td>
<td></td>
</tr>
<tr>
<td>02</td>
<td>27 F, R M</td>
<td></td>
<td></td>
</tr>
<tr>
<td>02</td>
<td>77 G, T</td>
<td></td>
<td></td>
</tr>
<tr>
<td>02</td>
<td>73 H, A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>03</td>
<td>64 S, C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>02</td>
<td>79 S, A S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>02</td>
<td>40 W, J E I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>03</td>
<td>74 W, C L</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **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.1799G>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)

- 0 variants (11.8%)
- 1 variant (29.6%)
- 2 variants (31.8%)
- 3 variants (18.4%)
- 4 variants (6.6%)
- ≥5 variants (1.9%)
Engaging patients
Engaging patients
Engaging patients

## Personalized Medicine

Each person responds differently to medicines. Your genes play a role in how you respond to medicines. Based on your history, your provider has ordered a test to learn more about which drugs are right for you. Having this information can help predict and prevent bad drug side effects.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Does your genetic test result affect your response to medicines?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel/Plavix</td>
<td>Yes</td>
</tr>
<tr>
<td>Simvastatin/Zocor</td>
<td>Yes</td>
</tr>
<tr>
<td>Tecrolimus</td>
<td>No</td>
</tr>
<tr>
<td>Thiopurine Therapy</td>
<td>No</td>
</tr>
<tr>
<td>Warfarin/Coumadin</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**The Clopidogrel Test**

Clopidogrel (sounds like "Kid-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

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

EMR-informatics capabilities
- Privacy
- Electronic phenotyping
- Large populations
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

The eMERGE Network
Electronic Medical Records & Genomics
A consortium of biorepositories linked to electronic medical records data for conducting genomic studies.
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

Proportion prescribed drug within genotype group

- Poor Metabolizer: 53% Clopidogrel, 47% Prasugrel
- Intermediate Metabolizer: 79% Clopidogrel, 21% Prasugrel
- Indeterminate: 93% Clopidogrel, 6% Prasugrel
- Normal: 94% Clopidogrel, 6% Prasugrel

“Final” therapy:
- Clopidogrel
- Prasugrel
- Ticagrelor

N=32 (Poor Metabolizer), N=305 (Intermediate Metabolizer), N=122 (Indeterminate), N=1079 (Normal)