

Integrating the Genome into the Electronic Health Record: The Next Leap Forward

**John Glaser, PhD
Vice President and CIO
Partners HealthCare**

May 8, 2008

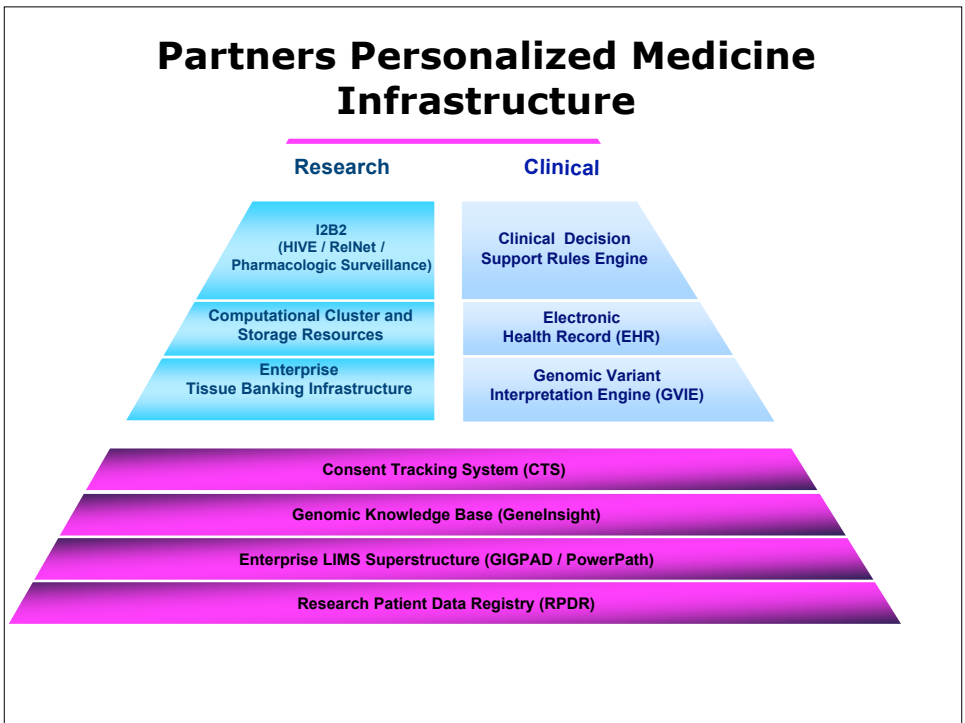
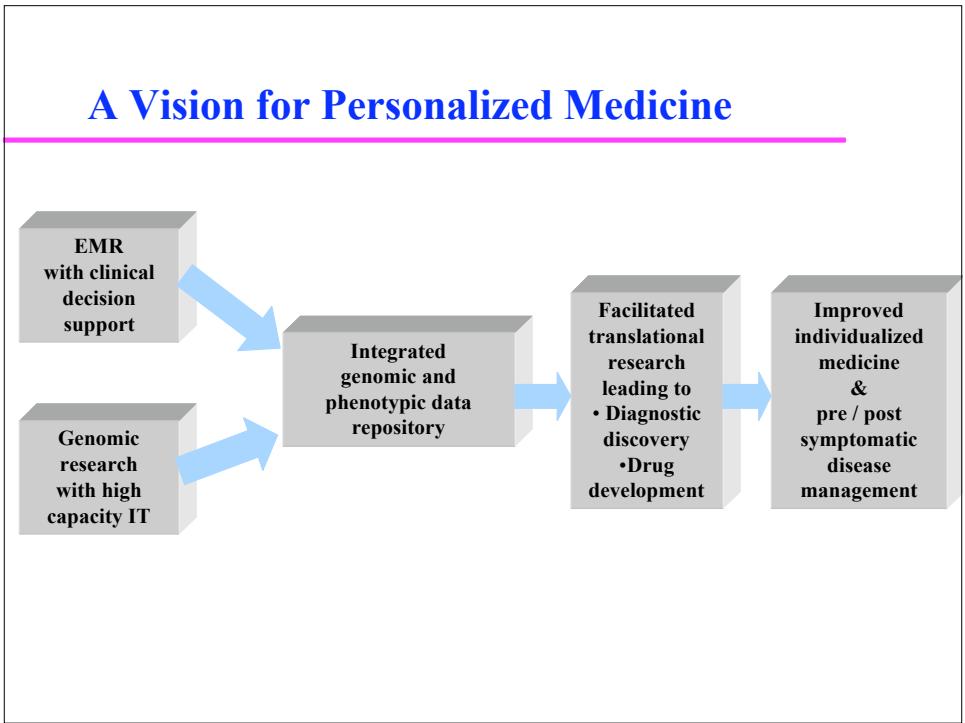
Clinical and Research Questions

◆ **Research**

- Why do some patients with asthma respond to steroid treatment while others do not?
- Why does a mutation in Huntington's gene cause a lethal defect?
- Why do some patients with diabetes have few complications even with "poor" control whereas others with good control have severe complications?

◆ **Clinical**

- Can I lower my cholesterol by diet alone or should I start on an anti-cholesterol drug now?
- Will a third line anti-cancer drug be more effective as a first line drug with a patient with lung cancer?

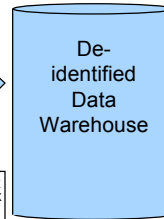
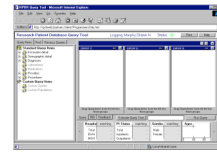


RPDR Allows Exploration and Delivery of Clinical Data

1) Queries for aggregate patient numbers

- Warehouse of in & outpatient clinical data
- 4.1 million Partners Healthcare patients
- 1 billion diagnoses, medications, procedures, laboratories, & physical findings coupled to demographic & visit data
- Authorized use by faculty status
- Clinicians can construct complex queries
- Queries cannot identify individuals, internally can produce identifiers for

Query construction in web tool

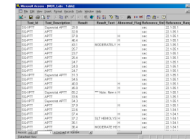
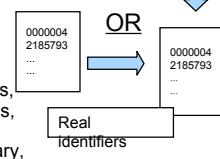


Encrypted identifiers

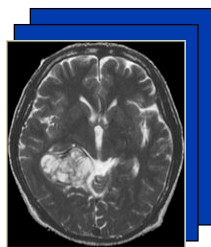
Z731984X
Z74902XX

2) Returns identified patient data

- Start with list of specific patients, usually from (1)
- Authorized use by IRB Protocol
- Returns contact and PCP information, demographics, providers, visits, diagnoses, medications, procedures, laboratories, microbiology, reports (discharge, LMR, operative, radiology, pathology, cardiology, pulmonary, endoscopy), and images into a Microsoft Access database and text files.



Structuring Unstructured Image Data

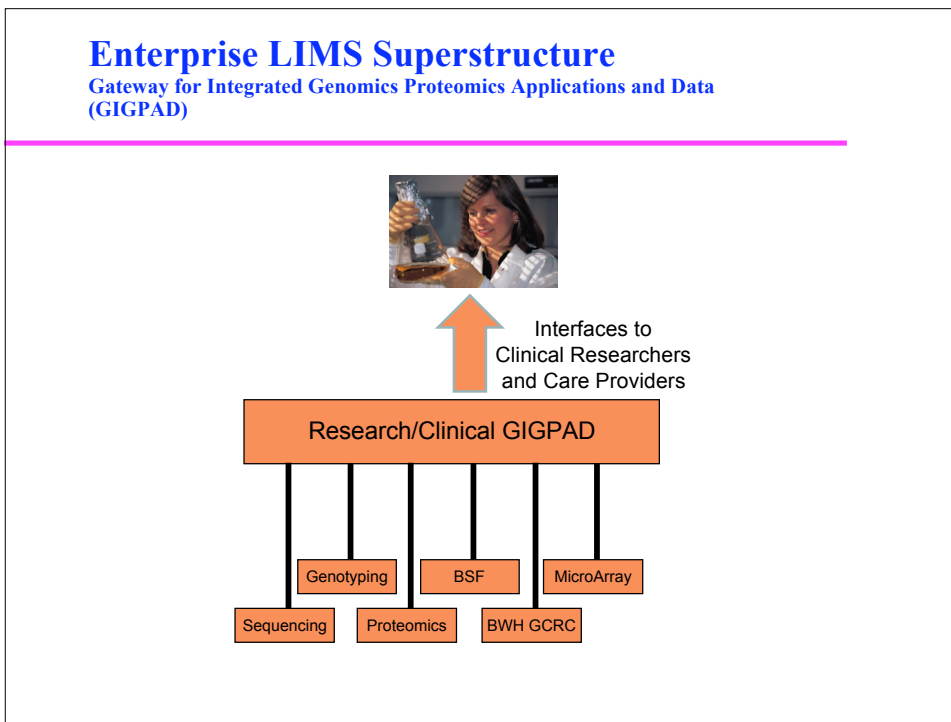


◆ Classifying Interpreted Findings

- LEXIMER (Lexicon Medical Entropy Reduction)
- Codification - CPT, ICD-9, RADLEX, SNOMED

◆ Image Feature Extraction

- Modern CAD Applications
 - » CT Chest
 - ◆ Lung Nodule Detection
 - » Digital Mammography
 - ◆ Cancer Detection
- Future Applications
 - » Brain CT, MRI
 - ◆ Sagittal asymmetry index, Tumor detection
 - » Cardiac MRI, US, NM
 - ◆ Myocardial wall thickness quantification
 - » Future Imaging Modalities
 - ◆ Molecular, THz, OCT, 3D Imaging



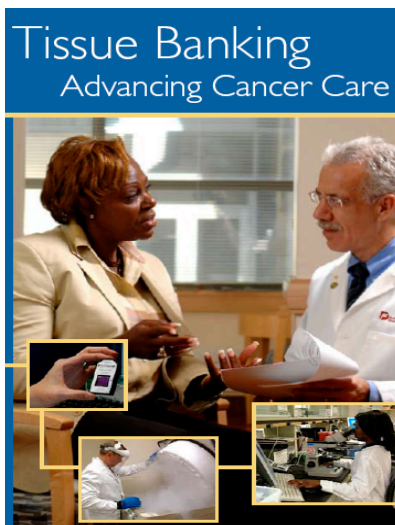
GeneInsight - DNA Variant Knowledgebase

*** Variant Status: (P) Pending Review, (V) Not Valid, (C) Confirmed, (W) Has Notes
34 variants found, displaying all variants
Export options: CSV | Excel | XML | PDF

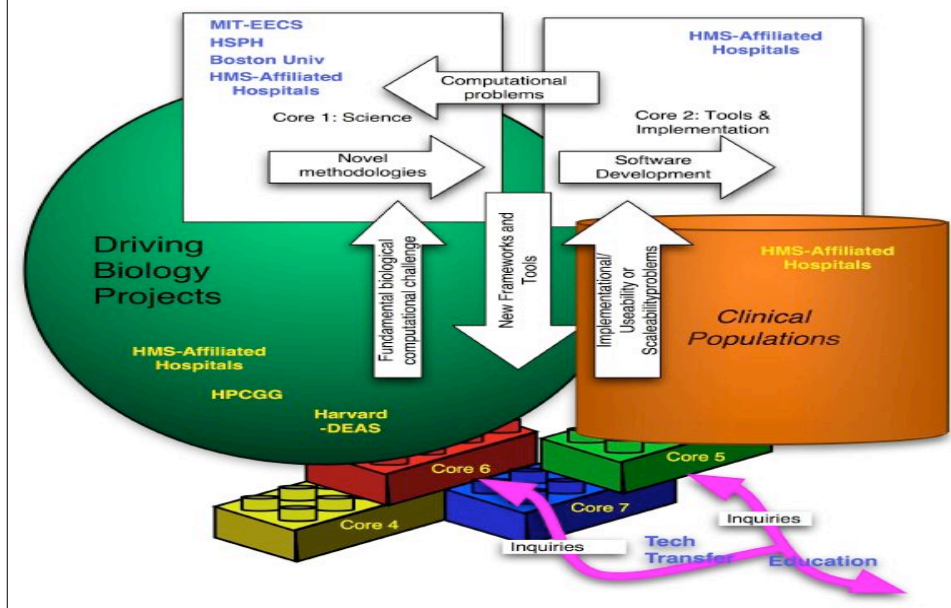
Gene	Allele	DNA	AA	Region	Category	Dis
TGFB2	170-2A>G			Intron 1	Pathogenic	MFS, LDS, TAAD
TGFB2	571G>A	V191I		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	773T>G	V258G		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	923T>C	L308P		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1006T>A	Y336N		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1063G>C	A355P		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1067G>C	R356P		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1069G>T	G357W		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1106G>T	G369V		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1151A>G	N384S		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1181G>A	C394Y		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1388T>G	C396W		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1395G>A	V387L		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1273A>G	M425V		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1322C>T	S441F		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1336G>A	D446L		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1346C>T	S449F		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1378C>T	R460C		Exon 4	Pathogenic	MFS, LDS, TAAD
TGFB2	1379G>A	R460H	R	Exon 5	Pathogenic	MFS, LDS, TAAD

Pannu et al, 2005

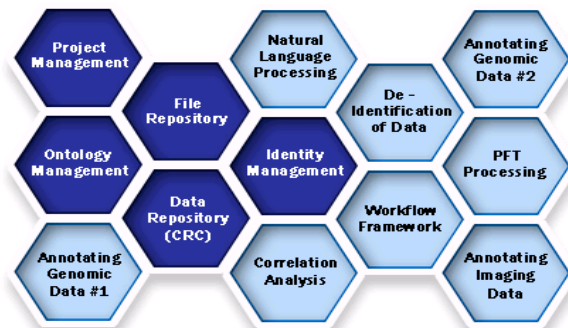
Tissue Sample Collection



Informatics for Integrating Biology and the Bedside (I2B2)

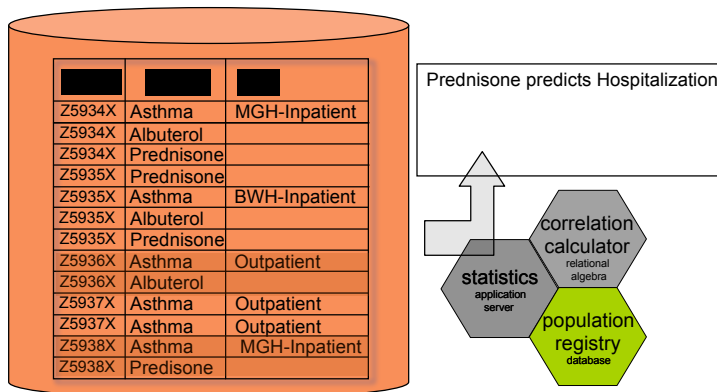


i2b2 Hive



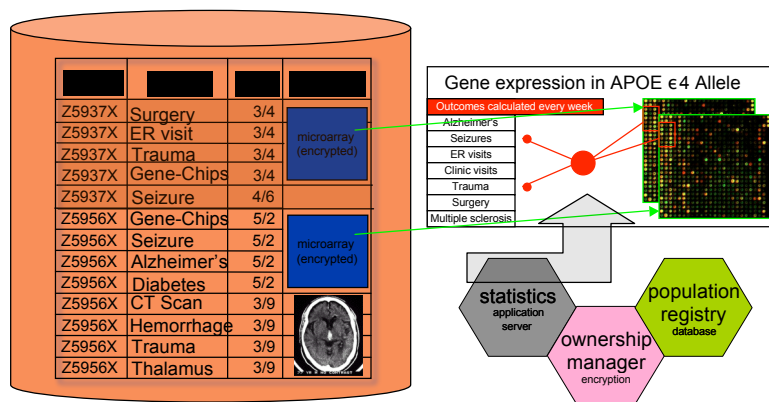
Predictive Modeling

Predicting future hospitalizations from prior use of medications in patients that have Asthma:



Clinical Trials Performed In-Silico

Clinical trial performed exclusively in computer memory finds APOE epsilon 4 allele determines risk of seizures after trauma



Key Personalized Medicine EHR Functions

Proper Display of Genetic/Genomic Information

Maintenance of Patient Genetic Profile

Real Time Clinical Decision Support

Population Based Clinical Decision Support

Knowledge Event Propagation

PM CDS

- ◆ Patient genetic profile summary view
- ◆ Disease based clinical views of genotypic and phenotypic data (e.g. Breast Cancer vs. Diabetes)
 - Leverage complete genetic profile in CDSS
 - Translate genetic profile into clinical risk, diagnosis, and pharmacogenomic guidance.
- Drug – Genetic Intervention alert, when medication is contraindicated or another is more efficacious
- Genetic aware drug dosage calculators
- Identification of 'at risk' patient populations for prophylaxis and screening programs
- Monitoring patient profile for high-risk situations
- Maintaining clinical validity and utility of patient genetic profile over time with changing knowledge, and alert clinician to changes in recommendations

Electronic Health Record

0000004 MGH Claus,Santa C, Jr. - Genetics Summary - Microsoft Internet Explorer provided by Partners HealthCare System

Sites: MGH BWH ALL

Date	Site	Primary Specimen	Indication	Test	Status
06/27/2006	MGH	Lung - Fixed Tissue	Pharmacogenomic	EGFR: b	Amend/Addenda
06/27/2006	MGH	Blood, Peripheral	Family History	HCM-pn1B , UCH-pn1A , HCM-pn1A	Final
06/27/2006	MGH	Blood, Peripheral	Family History	CX2B-a , CX3U-a , DFNMT-pn1A , COCH-a , POUSF4-a , MYO7A-a , PDS-a	Final
No mutations detected.					
06/27/2006	MGH	Blood, Peripheral	Pharmacogenomic	EGFR: b , EGFR: a	Final
06/26/2006	MGH	Fixed Tissue/Block (Lung) for EGFR	Pharmacogenomic	EGFR: a	Final
2235_2243del (E746_R748del), Exon 19, EGFR					

Genetics Clinical Decision Support

Select Desktop **PT Chart: Medications** Oncology Custom Reports Admin Sign Results ? Resc

Warning

You are ordering: **TARCEVA (ERLOTINIB)**

Drug - Genetic Intervention

Alert Message Keep New Order - select reason(s)

TARCEVA (ERLOTINIB) is contraindicated in patients with a somatic EGFR mutation known to be associated with resistance to Tyrosine Kinase Inhibitors for treatment of non-small cell lung cancer.

Most recent = Resistant 12/21/2006

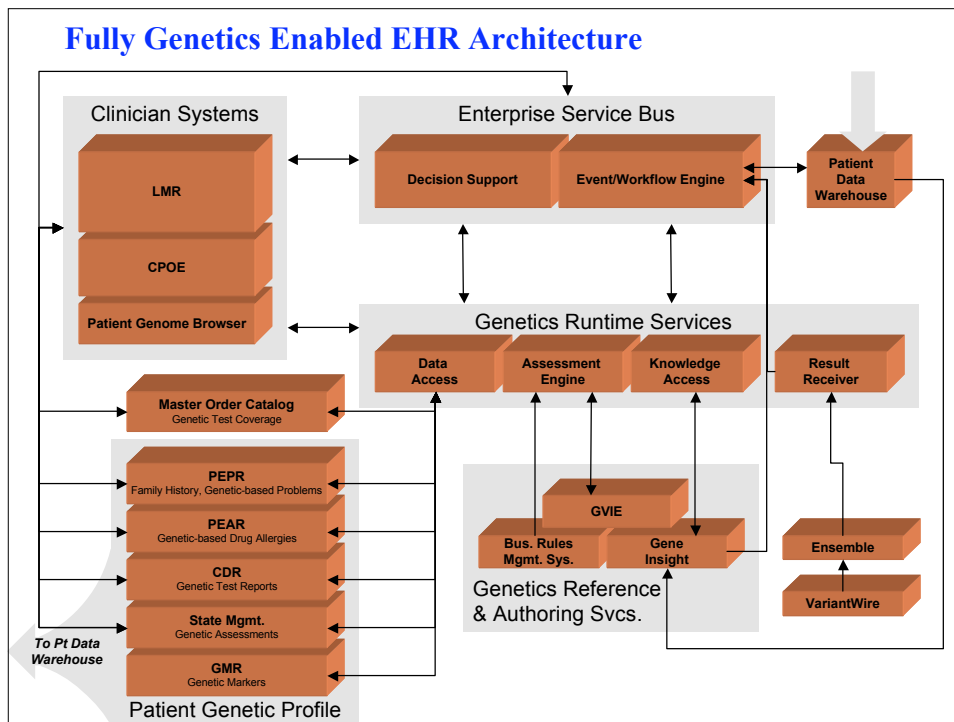
See Report in Genetics Summary under Results

Reasons for override:

Patient has pancreatic cancer

No reasonable alternatives

Other



Summary

- ◆ Personalized medicine will become an integral part of care delivery
- ◆ Partners has begun to implement the information technology foundation needed to support:
 - Research into the genomic bases of disease
 - Care delivery based on knowledge of a patient’s genome