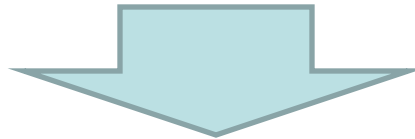


Challenges in Developing Healthcare IT Data Standards for Genomics

Mollie Ullman-Cullere
Dana-Farber Cancer Institute and Partners Healthcare
NHGRI Workshop
Genomics and HIT systems: Exploring the issues
April 27-28, 2011

Requirements for Genetic/Genomic Data in Clinical Care

- Accessible in the EHR as Structured Data
- Integrated into Clinical Workflows
- Available to Clinical Decision Support
- Integrated into Data Warehouses
 - patient panel management, outcomes analysis, quality assurance, reporting and discovery research
- Maintained Up-to-Date Interpretations



Function Like Other Laboratory Test Results

Select Desktop Pt Chart: Summary Oncology Custom Reports Admin Sign Results ? Resource Popup

Reminders
- Patient has H/O Angiogram problem list and aspirin is not on the medication list. Recommend a

Flowsheets

Medications

Abiraterone 300
Acetaminophen
Amoxicillin
Benadryl (DIPHENHYDRAMINE) 50 MG (50MG TABLET tak
Children's Tylenol (PARACETAMOL) 100MG/5ML ORAL LIQUID (IBUPROFEN
Lipitor (ATORVASTATIN) 10 MG (10MG TABLET take 1) PO
Lasix (FUROSEMIDE) 40 MG (40MG TABLET take 1) PO QD
Levaquin (LEVOFLOXACIN) 500 MG (500MG TABLET take 1) PO
Lipitor (ATORVASTATIN) 20 MG (10MG TABLET take 2) PO
Methenamine HIPPURATE 1 GM (1G TABLET take 1) PO BI
Neurontin (GABAPENTIN) 100MG CAPSULE PO as directed

Procedures Add New

Physicians Add New

Notes Add New

Reminders: Early Detection Screens for Risk Reduction

Medications: Pharmacogenomic Implications to Therapy

Problems

Above knee amputation
Pr pronic inflammatory disease - Major
Pr elevated cholesterol - Minor
Diabetes mellitus type 2
Gastroesophageal reflux disease
R/o fatty liver disease
Chronic obstructive pulmonary disease
H/o congestive heart failure - Major
H/o alcohol abuse - Major

Oncology: Tumor Genomic Profiling

Problem List: Genetic Diagnosis, Sub-typing and Risk

Health Maintenance

Care Providers Add New

Advance Directives

Pharmacies

Patient M/A List

Oncpro

Customize

Family History Add New

Family History Problem Relative

Allergies: Toxicogenomic Implications to Therapy

Genetics Summary: Patient's Genetic Profile

Family History: Risk Assessment and Phenotype Analysis

Genetic - Drug Interaction Alerts: Pharmacogenomic/Toxicogenomic Knowledge Alerts

Warning
You are ordering TARCEVA (ERLOTINIB)
Drug - Genetic Interaction
Alert Message
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.
Reasons for override:
 Patient has pancreatic cancer
 No reasonable alternatives
 Other
Most recent - Resistant 12/12/06
See Report in Genetics Summary under Results
Continue New Order Cancel Back To Lookup

Visits
Date
01/19/05 12:00
10/12/04 07:00
09/25/01 12:00 RYAN, DANIEL P., M.D.

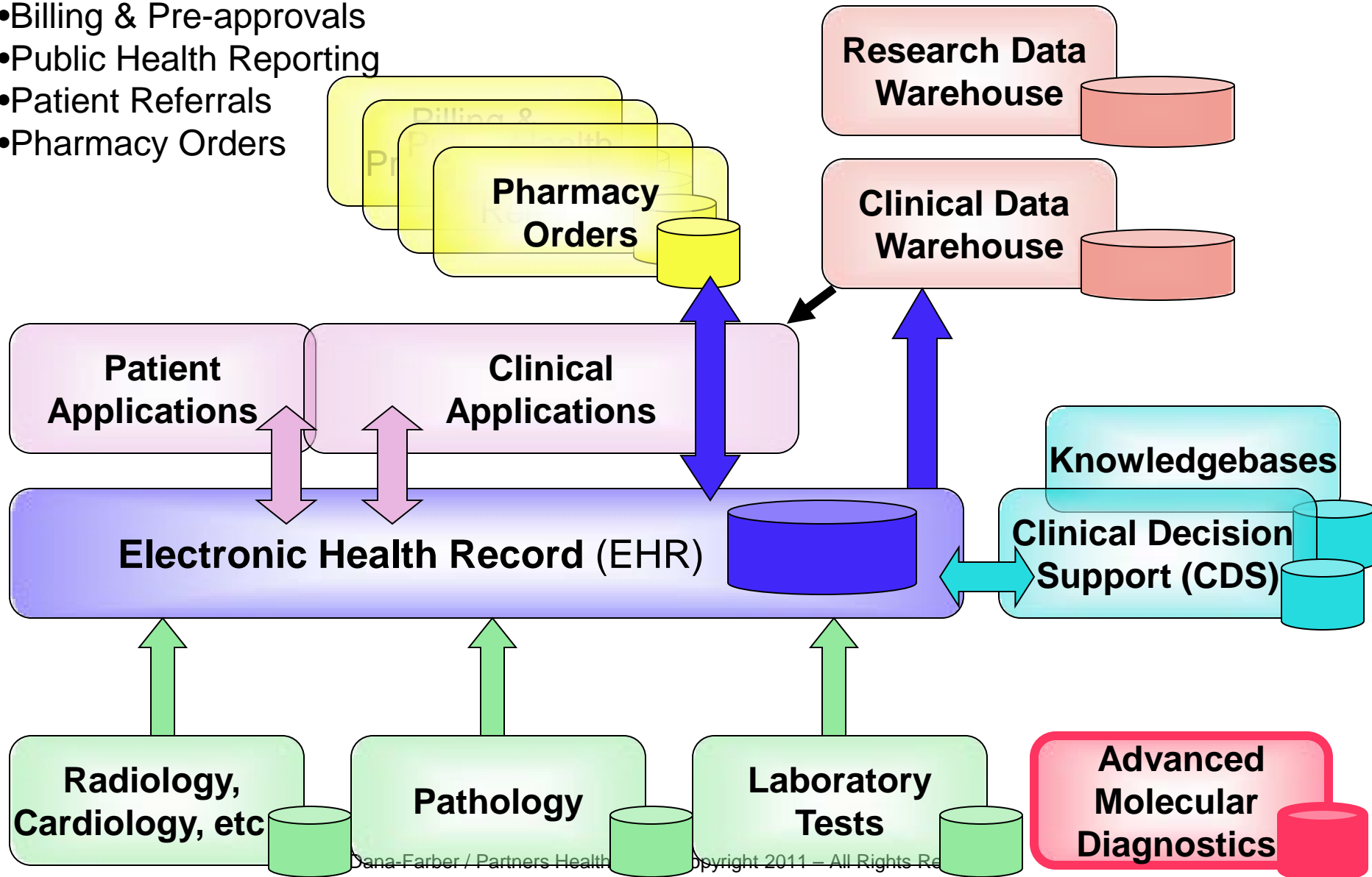
Genetics Summary
Phylaxis
Phylaxis
Phylaxis
Phylaxis
Status Change
Advance

Local intranet

Electronic Health Record (EHR) – Components & Data Flow

External Communications:

- Billing & Pre-approvals
- Public Health Reporting
- Patient Referrals
- Pharmacy Orders



How do we not make this a picture of Genomic Medicine and Healthcare?



Butler, D. *Translational Research: Crossing the Valley of Death*. *Nature* 453, 840-842 (2008)

Current HIT Clinical Genomics Data Standards

Ensure transfer of data between systems ...

Health Level Seven – HL7

Ensure standard description of tests, results, and interpretations ...

LOINC, Logical Observation Identifiers Names and Codes
HGVS Nomenclature, Human Genome Variation Society
HGNC, Human Gene Nomenclature Committee
RefSeq, Reference Sequences NCBI
dbSNP. Single Nucleotide Polymorphism
ISCN, International Society for Cytogenetics Nomenclature

Ensure standard context for interpretations (i.e. associations) ...

SNOMED & RxNORM

Other References

LRG, OMIM, COSMIC, PubMed...

Portion of LOINC Panel for DNA Variant Details

| LOINC Code | Name | Example value | source |
|------------|---|--|-------------------|
| 51958-7 | Transcript Reference Sequence Identifier | NM_005228.3 | NCBI DB |
| 48018-6 | Gene identifier | EGFR | HGNC Nomenclature |
| 48004-6 | DNA Sequence Variation | c.2573T>G | HGVS Nomenclature |
| 48003-8 | DNA Sequence Variation identifier | rs121434568 | NCBI dbSNP |
| 48002-0 | Genomic source class | Somatic , Likely Somatic, Unknown Origin, Likely Germline, Germline | LOINC Answer List |
| 51961-1 | Drug efficacy sequence variation interpretation | Resistant, Responsive , Presumed Resistant, Presumed Responsive, Unknown Significance, Benign, Presumed Benign, Presumed Non-Responsive | LOINC Answer List |

Portion of HL7 Genetic Results v2 Message

Header

63-7^Medication assessed^LN||337525^Erlotinib^RxNorm|||||F|20080702100909|||||Laboratory for Molecular
Medicine^L^22D1005307^^CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B

02-0^Genomic source class^LN||LA6684-0^Somatic^LN|||||F|20080702100909|||||Laboratory for Molecular
Medicine^L^22D1005307^^CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B

OBX|3|CWE|51964-5^Drug efficacy analysis overall interpretation^LN||^LA6677-4^Responsive^LN|||||F|20080702100909|||||Laboratory for Molecular
Medicine^L^22D1005307^^CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B

OBX|4|FT|51969-4^Genetic analysis summary report^LN||... <Report Text>

Findings (repeat panel as needed)

5^Genetic analysis discrete result panel^LN|||||20080702000000|||||20080702000000|||||

OBX|4|PM-08-Q00228-3^HPCGG-LMM^2.16.840.1.113883.3.167.1^ISO|55208-3^DNA analysis discrete sequence variation panel^LN|||||20080702000000|||||20080702000000|||||20080702000000|||||Q00228-2&HPCGG-LMM&2.16.840.1.113883.3.167.1&ISO

OBX|1|CWE|48018-6^Gene identifier^LN||3236^EGFR^2.16.840.1.113883.6.281|||||F|20080702100909|||||Laboratory for Molecular
Medicine^L^22D1005307^^CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B

OBX|3|CWE|51958-7^Transcript reference sequence identifier^LN||NM_005228.3^2.16.840.1.113883.6.280|||||F|20080702100909|||||Laboratory for Molecular
Medicine^L^22D1005307^^CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B

OBX|4|CWE|48003-8^DNA sequence variation Identifier^LN||rs121434568^99HPCGG-LMM-MARKER|||||F|20080702100909|||||Laboratory for Molecular
Medicine^L^22D1005307^^CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B

OBX|5|CWE|48004-6^DNA sequence variation^LN||c.2573T>G
^2.16.840.1.113883.6.282|||||F|20080702100909|||||Laboratory for Molecular Medicine^L^22D1005307^^CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B
Exon 19|||||F|20080702100909|||||Laboratory for Molecular Medicine^L^22D1005307^^CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B

OBX|10|CWE|48002-0^Genomic source class^LN||LA6684-0^Somatic^LN|||||F|20080702100909|||||Laboratory for Molecular
Medicine^L^22D1005307^^CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B

OBX|11|ST|47998-0^DNA sequence variation display name^LN||
c.2573T>G (p.Leu858Arg), Exon 21, EGFR, Responsive|||||F|20080702100909|||||Laboratory for Molecular
Medicine^L^22D1005307^^CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B

OBX|12|CWE|51961-1^Drug efficacy sequence variation interpretation^LN ||1|LA6677-4^Responsive^LN|||||F|20080702100909|||||Laboratory for Molecular
Medicine^L^22D1005307^^CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane^Ste. 123^Cambridge^MA^99999^USA^B

Co-Create Human Readable & Computer Readable Elements for the EHR

Launched August 2006

Launched March 2007

Alert Message
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

You are ordering: **TARCEVA (ERLOTINIB)**
Warning: Drug - Genetic Intervention

Reasons for override:
 Patient has pancreatic cancer
 No reasonable alternatives
 Other: _____

Continue New Order Cancel Back To Lookup Keep New Order - si

| Indication | Test |
|-----------------|---|
| Pharmacogenomic | EGFR |
| Family History | HCM.pnR, UCH.pnA, HCM.pnD |
| History | 565G>A (V189), Exon 5, MYBPL, CCG-a, CCG-x, DFNM, pnA, CCG-x, ... |
| | No mutations detected. |
| | EGFR, EGFR |
| Pharmacogenomic | 2156G>C (G719A), Exon 18, EGFR |
| | EGFR |
| | 2235_2236del (E746_R748del), Exon 19, EGFR |

MOLECULAR DIAGNOSTIC REPORT

REPORT INFORMATION

TEST INFORMATION

OBX[8]CWE|48006-1*Amino acid change type*LN||LA6692-3Deletion*LN|||||F|20080702100909|||||Laboratory for Molecular Medicine*L^22D1005307^*CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane*Ste. 123*Cambridge*MA^99999^USA^B

OBX[9]CWE|47999-8*DNA region name*LN||*Exon 19|||||F|20080702100909|||||Laboratory for Molecular Medicine*L^22D1005307^*CLIA&2.16.840.1.113883.4.7&ISO|1000 Laboratory Lane*Ste. 123*Cambridge*MA^99999^USA^B

This slide is intended to illustrate general IT functionality.
 Content displayed is not intended for clinical use.
 Screen configurations may not reflect the current version of the application

HL7 Implementation Guides for Structuring Clinical Genetic Test Results within Established Standards

Published

- Gene Variants associated with Disease/Risk, Drug Metabolism and Drug Efficacy

In Ballot

- Cytogenetics and Array CGH
- Genetic Test Report (*alt. format for transmission of codified findings*)

Under Development

- Gene Variants for Tumor Profiling
- Expression Profiling

Piloting Organizations

- Healthcare Providers: Partners Healthcare, Dana-Farber/Brigham and Women's Cancer Center, and Intermountain Healthcare
- Laboratories: Laboratory for Molecular Medicine at Partners Healthcare, Dana-Farber/Brigham and Women's Cancer Center at Harvard Medical School, and ARUP Laboratories at University of Utah

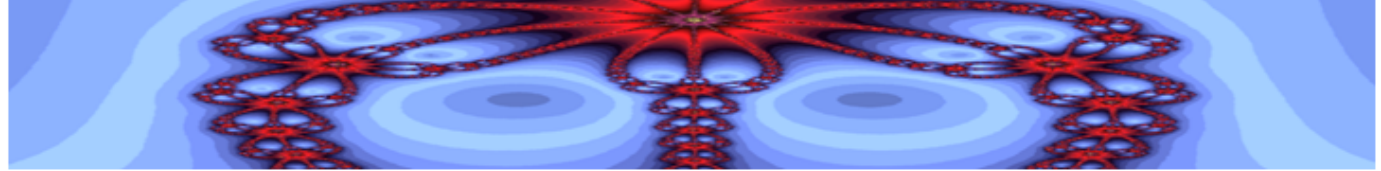
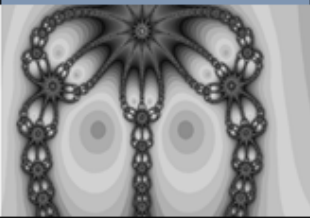
What's Needed for Standards Development?

Roadmap, Pilot Projects, Tools,
Collaborators, and Community
Involvement

Healthcare IT (HIT) Standards Development Best Practices

1. Participate in the healthcare standards communities (HIT and Genetics), as well as national initiatives
 - Participate in community review and publication (which is a separate track from journal publication).
 - Use tools for generation/translation/validation into standard representation e.g., HGVS's Mutalyzer tool:
<http://www.mutalyzer.nl/2.0/>
2. Align standards development and real-world implementation projects
 - Does it enable useful functionality while supporting professional, legal and policy requirements?
3. Collaborate with key stakeholders
 - **Vocabulary/Message Standards:** NCBI, NLM, HGVS, HL7 and LOINC
 - **Practitioners:** Geneticists, clinicians, pathologists, and molecular diagnostic laboratories
 - **IT Professionals:** EHR, Clinical Research, Bioinformatics, and LIMS Developers

Mutalyzer – HGVS Nomenclature Name Generator/Checker/dbSNP Converter



[previous page](#)

[home](#) [about](#) [contact](#) [go to bottom](#)

Mutalyzer 2.0 β -8

released on 31 Jan 2011

HGVS nomenclature version 2.0

Welcome to the Mutalyzer web site

The aim of this program suite is to support checks of sequence variant nomenclature according to the [guidelines](#) of the [Human Genome Variation Society](#).

Different interfaces are provided to collect the information necessary for the checks:

- The [Name Checker](#) takes the complete sequence variant description as input and checks whether it is correct.
- The [Syntax Checker](#) takes the complete sequence variant description as input and checks whether the syntax is correct.
- The [Position Converter](#) can convert chromosomal positions to transcript orientated positions and vice versa.
- The [GenBank Uploader](#) allows you to upload and use your own reference sequence.
- The [SNP converter](#) allows you to convert a dbSNP rsId to HGVS notation.
- The [Webservices](#) page provides instructions for the webservices.
- The [Batch Checkers](#) are interfaces that accept a list of inputs. These interfaces can be used for large quantities of checks.

GenBank sequences are retrieved from the [NCBI](#) ([Copyright and Disclaimers](#)).

This project is sponsored by [SUN Microsystems](#) with server hardware within the scope of the Academic Excellence Grant (AEG) program (award EDUD-7832-080223-CNE).

- Home
- Name Checker
- Syntax Checker
- Position Converter
- SNP Converter
- Name Generator
- Batch Jobs
 - Name Checker
 - Syntax Checker
 - Position Converter
 - SNP Converter
- GenBank Uploader
- Webservices
- Help
- FAQ
- Exercise
- Disclaimer
- Feedback

NCBI's dbSNP – Enhanced for the Clinical Perspective

NCBI Single Nucleotide Polymorphism

PubMed Nucleotide Protein Genome Structure PopSet Taxonomy OMIM Books SNP

Search for SNP on NCBI Reference Assembly

Search Entrez SNP for [] Go

Reference SNP(refSNP) Cluster Report: rs113488022 *Clinical Source**

| RefSNP | Allele | HGVS Names |
|--|-------------------------------------|--------------------------|
| Organism: human (Homo sapiens) | SNP: single nucleotide polymorphism | NG_007873.1:g.176429T>A |
| Molecule Type: Genomic | RefSNP Alleles: A/C/T | NG_007873.1:g.176429T>C |
| Created/Updated in build: 132/132 | T:Germline | NM_004333.4:c.1799T>A |
| Map to Genome Build: 37.1 | Allele Origin: A:Somatic | NM_004333.4:c.1799T>C |
| Validation Status: | C:Somatic | NP_004324.2:p.Val600Ala |
| | Ancestral Allele: T | NP_004324.2:p.Val600Glu |
| | Clinical Source: | NT_007914.15:g.1048759A> |
| | MAF/MinorAlleleCount: NA | |
| | MAE Source: | |

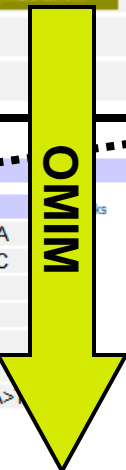
SNP Details are organized in the following sections:
GeneView Map Submission Fasta

Integrated Maps (Hint: click on 'Chr Pos' or 'Contig')

| Genome Build | Chr | Chr Pos | Contig |
|--------------|-------------------|---------------------------|------------------------------|
| 37.1 | 7 | 140453136 | NT_007914.15 |

GeneView
GeneView via analysis of contig annotation: [BRAF](#)
View more variation on this gene (click to hide).
Include clinically associated: in gene region

| Allele | |
|------------------------------|--------------------------------------|
| Variation Class: | SNP: single nucleotide polymorphism |
| RefSNP Alleles: | A/C/T |
| Allele Origin: | T:Germline A:Somatic C:Somatic |
| Ancestral Allele: | T |
| Clinical Source: | VarView OMIM |
| MAF/MinorAlleleCount: | NA |
| MAF Source: | |



.0001 MELANOMA, MALIGNANT, SOMATIC [BRAF, VAL600GLU] [dbSNP:rs113488022](#)

COLORECTAL CANCER, SOMATIC, INCLUDED, THYROID CARCINOMA, PAPILLARY, SOMATIC, INCLUDED, ASTROCYTOMA, LOW-GRADE, SOMATIC, INCLUDED

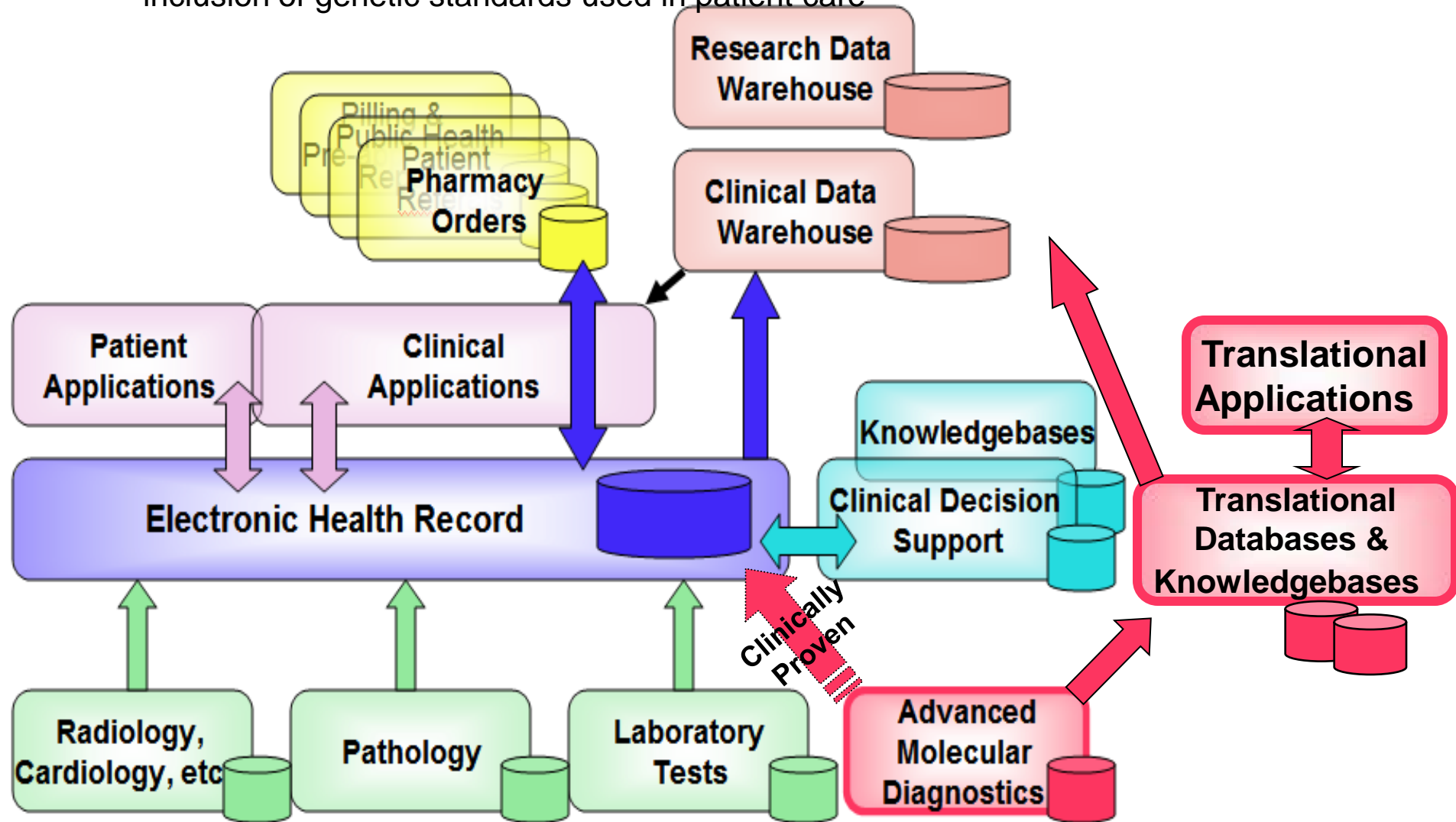
The val600-to-glu (V600E) mutation caused by a 1799T-A transversion in the BRAF gene was previously designated VAL599GLU (1796T-A). [Kumar et al. \(2003\)](#) noted that an earlier version of the BRAF sequence showed a discrepancy of 3 nucleotides in exon 1; based on the corrected sequence, they proposed a change in nucleotide numbering after nucleotide 94 (the ATG codon) by +3 and a corresponding codon change of +1. 💡

Malignant Melanoma

[Davies et al. \(2002\)](#) identified a 1799T-A transversion in exon 15 of the BRAF gene that leads to a val600-to-glu (V600E) substitution. This mutation accounted for 92% of BRAF mutations in

Translational Frameworks

- Adheres to HIT standards development best practices
- Focus on structured/codified data and terminologies extending HIT data standards for inclusion of genetic standards used in patient care



Recommendations to Extend Healthcare IT (HIT) Standards for Personalized Medicine

1. Define roadmap for parallel development of Electronic Health Records and Personalized Genomic Medicine

For example:

- Standard(s) for coding genetic based disease
 - Standard(s) for representation of genetic data (for human and computer consumption)
 - Minimal core data sets
 - Standard(s) for representation of clinical associations
 - Standard(s) for representation of clinical decision support rules
2. Fund tool development generating/translating/validating standard representation of data for Personalized Genomic Medicine (e.g. HGVS's Mutalyzer)
 3. Make HIT resources easier to find by listing published standards and implementation guides within PubMed
 4. Incorporate HIT standards into grants for genomic medicine