USING IT AND DATA-SHARING TO SCALE YOUR CLINICAL GENETICS PROGRAM

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GENETICS AND THE ROLE OF IT

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We believe that a best of breed solution is better than a monolithic, enterprise-wide solution because of our ability to focus and deliver solutions our clients need.
1. Biomarkers/genomic variants will be a primary tool

2. Patients and Physicians need Pathologists to interpret genomic information

3. Sunquest systems will store, analyze and provide decision support on genomic variants
OVERARCHING CLINICAL PROBLEM

• Every person has 3-5 million genetic variants
• We don’t know the implications of most variants but we are learning more every day
  – Interpretation/classification of a variant is not fixed and can change over time.
• How can clinicians keep up to date on the known implications of each variant in each patient?
• Current process and systems are not scalable for standard clinical care

More knowledge, variants, patients

More Interpretations to Perform
Solving scalability issues to make Genetics part of the standard of care

- Clinical Problem and Solution Vision
- IT Solutions
  - Integrated wet lab management
  - Continuously Learning Knowledge Management
  - Continuous Clinical Communication
- Real World Applications
  - Sunquest Molecular Module
  - GeneInsight at the Lab for Molecular Medicine
  - VariantWire® sharing network
SUNQUEST MOLECULAR MODULE

• Workflow-Protocol Authoring
  – Define complex protocols and tray map rules. Present workflow to end users in one application in a meaningful and interactive manner

• Inventory Management
  – Replace paper-based systems used to manage reagent inventory, master mix, cross checks, and availability as well as instrument/plant maintenance activity

• Enhanced QC
  – Address the unique QC challenges of MDX and LDTs with user-friendly graphic formats, enhanced trending, troubleshooting reports, and performance checklists

• Data Handling
  – Interface to rapidly changing instrumentation that does not conform to standard ASTM specifications

• Resulting and Reporting
  – Support interpretations in entering textual result or comments using combination of free and static text and attachments
INTEGRATION GOALS

• Enable Data Exchange
  – Allow structured data to be transferred between systems
  – Allow structured data and report to reach the EHR

• Reduce Manual Work and Potential Error
  – Reduce re-entry of data between systems
  – Prevent inconsistency between systems

• Deliver True Integration
  – Real time connections between systems
  – Patient Context

• Minimize Customizations
  – Standard supportable approach with various products
INTEGRATION POINTS

• Provide GeneInsight:
  – Demographic data (name, date of birth, gender)
  – Information about test(s) and specimen
  – AP case / Lab accession or CID
  – Changes to ADT or order
  – Variant call files from pipeline

• Provide LIS
  – Discrete data on reported variants and classifications
  – Signed off report from GeneInsight or report elements for finalizing

• Provide Clinicians:
  – Reports delivered by Sunquest via HL7 to EHR/EMR
  – GeneInsight Clinic (standalone or within EHR)
GOALS

- Integrate with clinical systems
- Manage complex workflows
- Incorporate tasks into standard workflow
- Reduce paper-dependent systems

*Integrated*
*Scalable*
*High Quality*
*Efficient*
CONFLICT OF INTEREST

Shana White is an employee of Partners HealthCare which has a partnership with Sunquest and a financial investment in GeneInsight Inc.
HOW DO WE INTRODUCE GENETICS TO THE BROADER COMMUNITY?

• 3 Billion Base Pairs of DNA Per Person
• 3-5 Million Variants Per Patient
• 22,000 Genes

Shock and Awe

Adopted from Sandy Aronson
This train is moving at 500 mph ....

But my healthcare training is moving at 2 mph.

Do you know what happens when you try to dock a 500 mph train to a 2 mph train?
The complexity and sophistication of this is incredible ....

But you get that I only have 15 minutes with each patient, right?
This gets me so excited about the future....

But is it really ready for prime time?
I am glad that a lot of smart people are thinking about this ....

But is there really any way that I am actually going to be able to apply it for my patients?

Is there any way I am going to be able to contribute to making this happen?
MAJOR COMPONENTS OF GENOMIC TESTS

Technical
(Analytical Validity)

Interpretive
(Clinical Validity)

Impact
(Clinical Utility)

Bottleneck in genomics

Inconsistency of methods
GENEINSIGHT SUITE

- In continuous clinical use since 2005
- Registered with the FDA as a class I exempt medical device
- Over 40,000 patient reports generated
STREAMLINED REPORTING PROCESS

Patient Details → Variant Filtration + Classification → Report Generation
GeneInsight
for better care

MENDEL, GREGORY

BIRTH DATE 1/1/2003
SEX Male
AGE 840
PEDIGREE

ACCESSION 8448

REFERRING PHYSICIAN
REFERRING FACILITY
REFERRING FACILITY MRN

GENEINSIGHT REPORT

TEST PERFORMED Pan Cardiomyopathy Panel (51 Genes)
INDICATION FOR TEST Cardiovascular Clinical diagnosis of HCM
RESULT Positive

DNA VARIANTS

MYH7, Heterozygous, c.2183C>T (p.Ala728Val), Path

HCM

DNA sequencing of the coding regions and splice sites of 51 cardiomyopathy genes (see methodology section below) identified the variant listed above.

Genetic testing of this individual's biological relatives, particularly those who are affected, may help to clarify the significance of this variant.

Cardiomyopathy due to pathogenic variants in the MYH7 gene is typically inherited in an autosomal dominant pattern. Each first-degree relative has a 50% (or 1 in 2) chance of inheriting a variant and its risk for cardiomyopathy. Disease penetrance and severity can vary due to modifier genes and/or environmental factors. The significance of a variant should therefore be interpreted in the context of the individual's clinical manifestations.

VARIANT INTERPRETATIONS:
This is an established pathogenic variant based on reports in the literature and >20 segregations in our internal laboratory data.

RECOMMENDATIONS
Genetic counseling is recommended for this individual and their relatives. Familial variant testing is available for other relatives if desired. For assistance in locating genetic counseling services or disease specialists, please call the laboratory at 817-768-8500 or email at LHM@partners.org.

INDIVIDUAL VARIANT INTERPRETATIONS

MYH7 Heterozygous c.2183C>T p.Ala728Val Pathogenic

COMMENTS

Common sequence variants of unlikely clinical significance that are classified as benign are not included in this report but are available upon request. In addition, the following less common sequence variant has been identified. Although it is likely benign we cannot rule out that it may be...
5 CHALLENGES IN SCALING THE GENETIC WORKFLOW

1. Organized and searchable database
2. Streamlined filtering
3. Real-Time access to external data
4. High quality, reliable reports
5. Comprehensive, ongoing patient care
DATA SHARING

Leveraging expertise in genomics
WHY HAS GENETICS EMBRACED DATA SHARING?

• The emergence of next generation sequencing has brought with it an increase in:
  – Quantity of sequencing data
  – Genes per test
  – Variants of uncertain significance

• Too much data for any one center to be an expert on all genes and genomic variations

• High expectations from the community to make genetic test results actionable

• Consistency across laboratories
DATA SHARING IN GENEINSIGHT

• Connectivity to public and private content
  – Ingenuity
  – dbSNP
  – ClinVar (Subgroup of ClinGen, supported by NIH)
    • Labs submit variants, classifications and structured justification
    • GeneInsight enables real-time access to data in ClinVar
    • Future enhancements include automated submission to ClinVar
• VariantWire
WHAT IS VARIANTRWIRE®?

- VariantWire is a **real-time** data sharing effort available to users of GeneInsight products.
- Sharing variant interpretations and gene-disease Relationships
- All shared variants are **clinically validated** and have been approved to be included on clinical reports
- All data is **de-identified** (void of any PHI)
- Policy and member selection is governed by the VariantWire Committee
  - Comprised of one member from each participating entity.
Clinically validated, de-identified, and approved data

Read-only viewing with ability to validate and import

<table>
<thead>
<tr>
<th>Shared Values</th>
<th>#</th>
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<tbody>
<tr>
<td>Labs</td>
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<td>Interpreted Variants</td>
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<tr>
<td>Diseases</td>
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HOW DO CLINICIANS INTERACT WITH GENETIC INFORMATION?
TYPICAL SITUATION

• Genetic test results are scattered through EHR

• Most results are not structured, organized or adequately interpreted for clinical use at point of care

• Significance of genetic variants change over time and clinicians are not updated as new knowledge emerges
<table>
<thead>
<tr>
<th>Report Identifier</th>
<th>Report Status</th>
<th>Report Date</th>
<th>Test</th>
<th>Overall Interpretation</th>
<th>Indication</th>
<th>Specimen</th>
<th>Genomic Source</th>
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<tbody>
<tr>
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<td>FINAL</td>
<td>03/26/2013</td>
<td>Pan Cardiomyopathy Panel (51 Genes)</td>
<td>Possibly Guided</td>
<td>Clinical diagnosis of HCM</td>
<td>No specimen recorded</td>
<td>Germline</td>
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</tbody>
</table>

**Variant**
- **Heterozygous c.301G>A (p.Glu101Lys), Exon 2, ACTC (Germline)**

**Current Category**
- **Pathogenic (03/26/2013)**

**Reported Category**
- **Unknown Significance**
75% of Geneticists believe there is an ethical obligation to re-contact the patient if new genetic information becomes available, regardless of time lapse.

ACMG 2014 poll
“Laboratories are encouraged to explore innovative approaches to give patients and providers more efficient access to updated information.”

ACMG Standards and guidelines for interpretation of sequence variants 2015
WITH GENEINSIGHT

GeneInsight Lab
• Automated and integrated genetics care from test order to patient results

GeneInsight Network
• Enables real-time connection for clinically validated variant interpretations

GeneInsight Clinic
• Comprehensive, ongoing patient care elevates the quality of care your institution provides
THANK YOU!

- Special thanks to our collaboration partners
- Thank you to the GeneInsight team and those at Partners HealthCare who support it
- For more information, please contact:
  marketing@sunquestinfo.com
  info@geneinsight.com