Touch-points for incorporating Genetic Data and Knowledge Into Clinical Processes
How Genetic Tests are Different

- Output is highly structured
- Volume of output is at times large – and the volume of output per test is growing
Typical HCM Workflow

Clinician identifies at risk patient

HCM Test Ordered

HCM Testing Laboratory

Test Performed

Interpretation Report

Variants of Unknown Significance

Known Variants

Clinician calls HCM lab to retrieve variant knowledge updates

Results and report sent direct to clinician

New Knowledge Discovered

DISCONNECT
Clinical Implications of Falling Sequencing Cost

- Test availability
- Test volume
- DNA assayed / test
- # variants identified / patient
- # of diseases assessed / test
- # variants with unknown or evolving clinical significance

Cost of Sequencing
Knowledge Management Challenges

**Lack of Automated Process to Update Provider when New Knowledge is Discovered**

- Knowledge Sources
  - Public Sources
  - Disease Correlations
  - Evidence Based Knowledge
  - ... per variant

**Interpretation Report Generated**

- Inconsistency in interpretation reports, inefficiency in report creation, inability to scale genetic testing practice

**Genetic Test Performed**

- Variant 1
- Variant 2
- Variant ...

**Test Results**

**Laboratories**

**Providers**

- Laboratory Sends Result
- Provider Receives Paper Report

- Laboratory Discovers New Knowledge

- Lack of Automated Process to Update Provider when New Knowledge is Discovered

- No ability to update test results as new knowledge is discovered on a previously tested patient

- Lack of structured data delivery to providers

- No knowledge management infrastructure to support process
Provider Infrastructure
The Most Important Touch Point is the Clinician Display

Data in this slide should not be used for any clinical purpose.
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Updated Variant Information

Data in this slide should not be used for any clinical purpose.
Laboratory Infrastructure
Data in this slide should not be used for any clinical purpose.
DNA sequencing of the coding regions and splice sites of the [TestGeneList] identified the variants listed above. No clinically significant DNA variants were detected in the other genes analyzed.

The presence of two pathogenic variants may lead to earlier onset and/or increased severity of disease. It would be important to determine whether these variants are present in cis (on the same copy of the gene) or in trans (on different copies) to understand the impact to the gene and accurately predict the risk to future offspring. This can be accomplished by testing this individual's biological parents. Please note that the laboratory can attempt testing on tissue specimens from deceased family members. It should be noted that the expression of [PatientDisease] is the product not only of a gene variant, but also of other modifier genes and environmental factors. The significance of a variant should always be interpreted in the context of the individual's clinical manifestations.

In summary, it is very likely that the one or both of these variants are causative of [PatientDisease] in this individual. The presence of two pathogenic variants may result in an earlier age of onset or more severe disease than one would expect if only one variant was present. However, the presence of only one of these variants is also likely to be sufficient to cause disease.

In summary, it is possible that the [MatchVariant 1 Amino Acid Change]: variant is primarily responsible for...
Variant Specific Categorization

Pathogenic
Likely Pathogenic
Unknown Significance
Likely Benign
Benign
+ Pharmacogenomic Categories

Data in this slide should not be used for any clinical purpose.
LIS Infrastructure
Manages Physical Process of Identifying Variants

Knowledge Base (GenelInsightSM)

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<th>Allele</th>
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<th>AA</th>
<th>Region</th>
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<td>G</td>
<td>G</td>
<td>Intron 1</td>
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<td>MPS, LDS, TAAO</td>
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</tbody>
</table>

Report Generation (GVIE)
Network Exchange Model

Organizations that generate patient genetic data and knowledge:
- Lab
- Lab
- Lab
- Knowledge Source
- Knowledge Source
- Knowledge Source

VariantWire℠/GenelInsight℠ Network

Organizations capable of generating incremental genetic knowledge (but currently lack an effective distribution mechanism):
- Provider
- Provider
- Provider

Organizations that need to maintain Patient Genetic Profiles with hybridized knowledge. Many are also able to generate/validate genetic knowledge:
- Provider
- Provider
- Provider
- Provider
- Provider
An Example Solution

Note: VariantWire does not yet support order entry
Key Standards Touch Points

- Providers
- Knowledge Providers
- Laboratories
- LIS
- Results Knowledge
- Interpretation
- Physical Test
- Order Entry
- Direct or Through EHR
- PGE
- VariantWire™
- GVIE / Genelnsight™
- Other Networks

Knowledge

Results Transfer

Patient Identification

Provider Interface
Looking Towards the Future and Setting Goals

Institution A

Genomic Discovery Made on Variant X
Doctor with Patient Harboring Variant X Receives Alert

World Wide

Doctor with Patient Harboring Variant X Receives Alert
Genomic Discovery Made on Variant Y

We should not allow this boundary to introduce a delay of more than a few minutes
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