VarSeq as a Clinical NGS Platform

April 15, 2015

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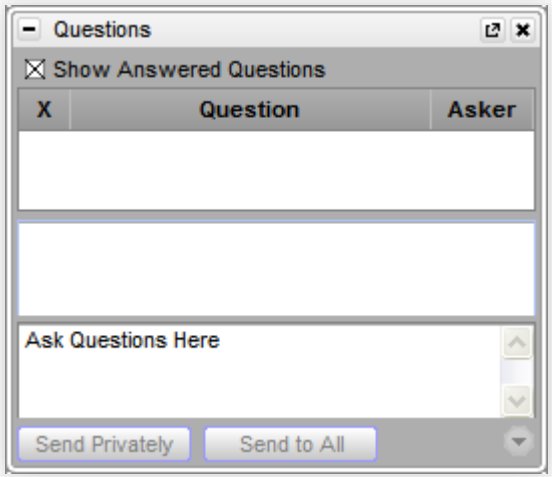
VP Product & Engineering

GOLDEN HELIX
Accelerating the Quest for Significance™

Questions during the presentation

Use the Questions pane in your GoToWebinar window



Agenda

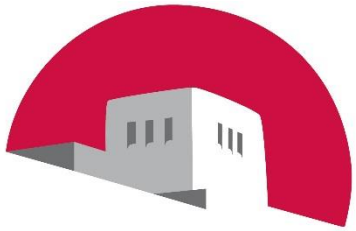
1. VarSeq and Clinical NGS Background
2. Workflows: What is it Capturing and How?
3. Knowledge Capture: Leveraging Insights
4. Prioritize: Best Candidates First

VarSeq Background

- **Golden Helix founded in 1998**
- **Work on VarSeq revealed in 2013**
- **VarSeq built on mature technology**
- **6 months since launch:**
  - Build out features to support clinical labs
  - Responsive to feedback

Stakeholders

- Jason Byars
- David Gokhale
- Kelly Eggleton
- Bruno Ping
- Cristian Ionescu-Zanetti
- Reece Hart
- Ken Kaufman
- Sam Strom
- Jeff Moore
- Jeff Rosenfeld
- Scott Ness



UNM

Liverpool Women's NHS Foundation Trust

FLUXION

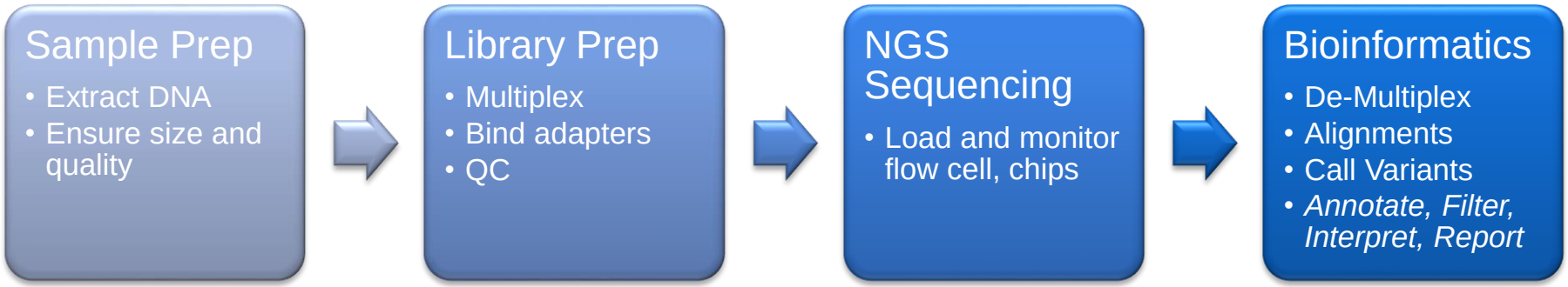
UCLA Health

Royal Surrey County Hospital NHS Foundation Trust

Cincinnati Children's®

ILLINOIS
UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

Laboratory Developed Tests

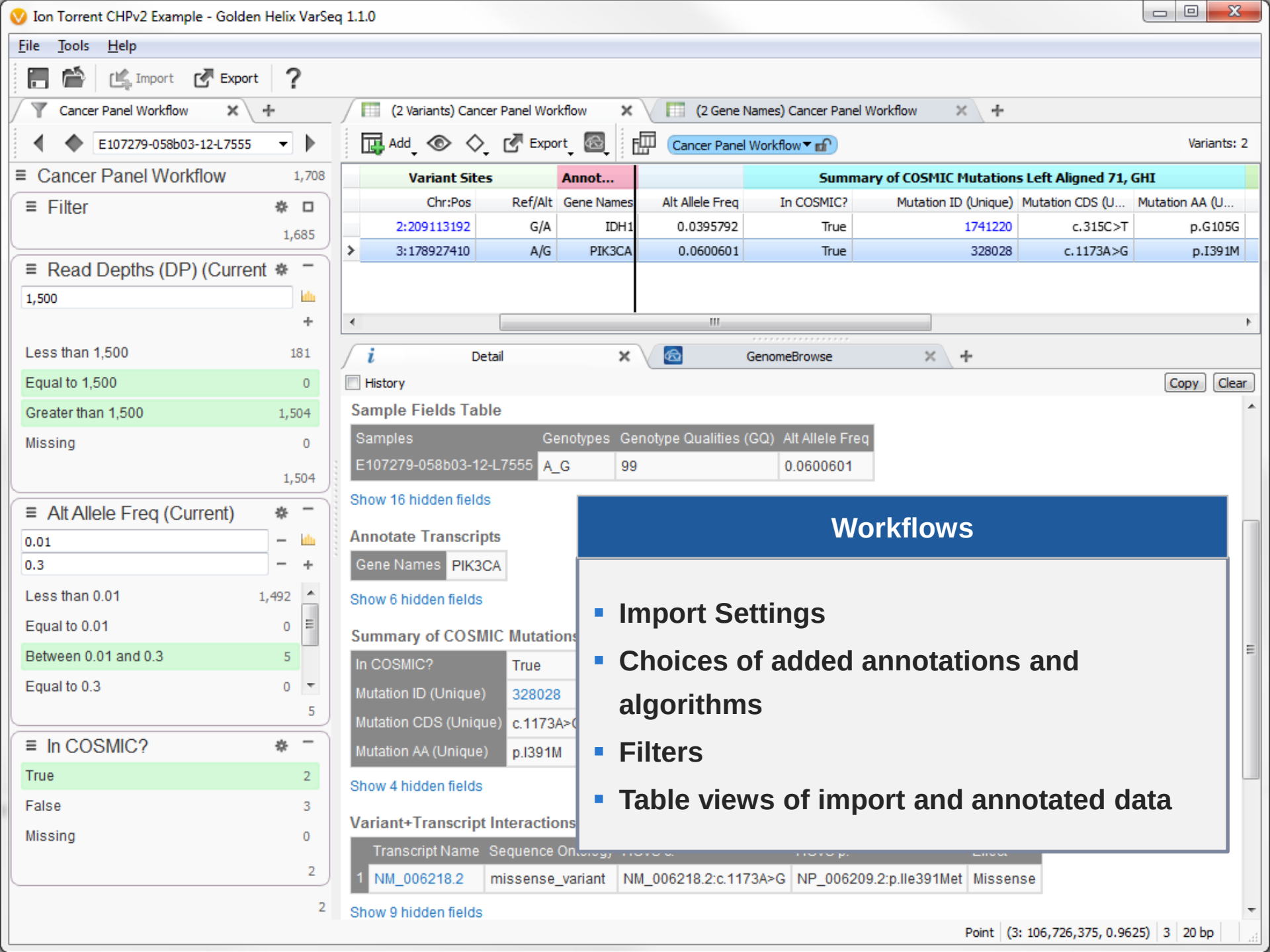


Applications

- Carrier Screening
  - CFTR, Prenatal/Preconception
- Hereditary
  - Cancer risk, Cardiomyopathy
- Pediatric/Diagnostic
  - Noonan Syn, Neuropathy, Epilepsy
- Cancer Gene Panels

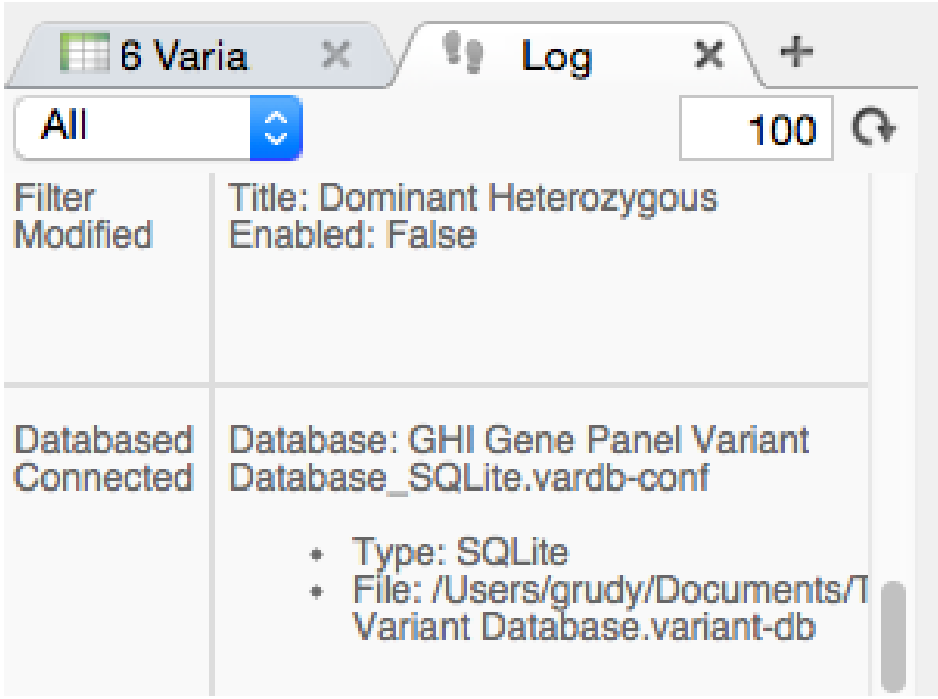
Economics

- Panels cheaper than single-gene tests
- Minimal hardware requirements
- Many off-the-shelf kits for popular tests
- Vender supported workflows
- *With correct interpretation workflow, can efficiently handle reporting/sign-off*


Ion Torrent CHPv2 Example - Golden Helix VarSeq 1.1.0
File Tools Help
Import Export
Cancer Panel Workflow
E107279-058b03-12-L7555
Cancer Panel Workflow 1,708
Filter 1,685
Read Depths (DP) (Current
1,500
Less than 1,500 181
Equal to 1,500 0
Greater than 1,500 1,504
Missing 0
1,504
Alt Allele Freq (Current)
0.01
0.3
Less than 0.01 1,492
Equal to 0.01 0
Between 0.01 and 0.3 5
Equal to 0.3 0
5
In COSMIC?
True 2
False 3
Missing 0
2
2
(2 Variants) Cancer Panel Workflow
(2 Gene Names) Cancer Panel Workflow
Add Export
Cancer Panel Workflow
Variants: 2
Variant Sites
Annot...
Summary of COSMIC Mutations Left Aligned 71, GHI
Chr:Pos Ref/Alt Gene Names Alt Allele Freq In COSMIC? Mutation ID (Unique) Mutation CDS (U... Mutation AA (U...
2:209113192 G/A IDH1 0.0395792 True 1741220 c.315C>T p.G105G
3:178927410 A/G PIK3CA 0.0600601 True 328028 c.1173A>G p.I391M
Detail
GenomeBrowse
History
Copy
Clear
Sample Fields Table
Samples Genotypes Genotype Qualities (GQ) Alt Allele Freq
E107279-058b03-12-L7555 A_G 99 0.0600601
Show 16 hidden fields
Annotate Transcripts
Gene Names PIK3CA
Show 6 hidden fields
Summary of COSMIC Mutations
In COSMIC? True
Mutation ID (Unique) 328028
Mutation CDS (Unique) c.1173A>G
Mutation AA (Unique) p.I391M
Show 4 hidden fields
Variant+Transcript Interactions
Transcript Name Sequence Ontology
1 NM_006218.2 missense_variant NM_006218.2:c.1173A>G NP_006209.2:p.Ile391Met Missense
Show 9 hidden fields
Workflows
Import Settings
Choices of added annotations and algorithms
Filters
Table views of import and annotated data
Point (3: 106,726,375, 0.9625) 3 20 bp

Workflows: What is it Capturing and How?

- Every project can be saved as as template
- Create New Projects with a template to reproduce with new data
- Everything logged, with precise details of what happened, by whom and when.



[Demonstration]

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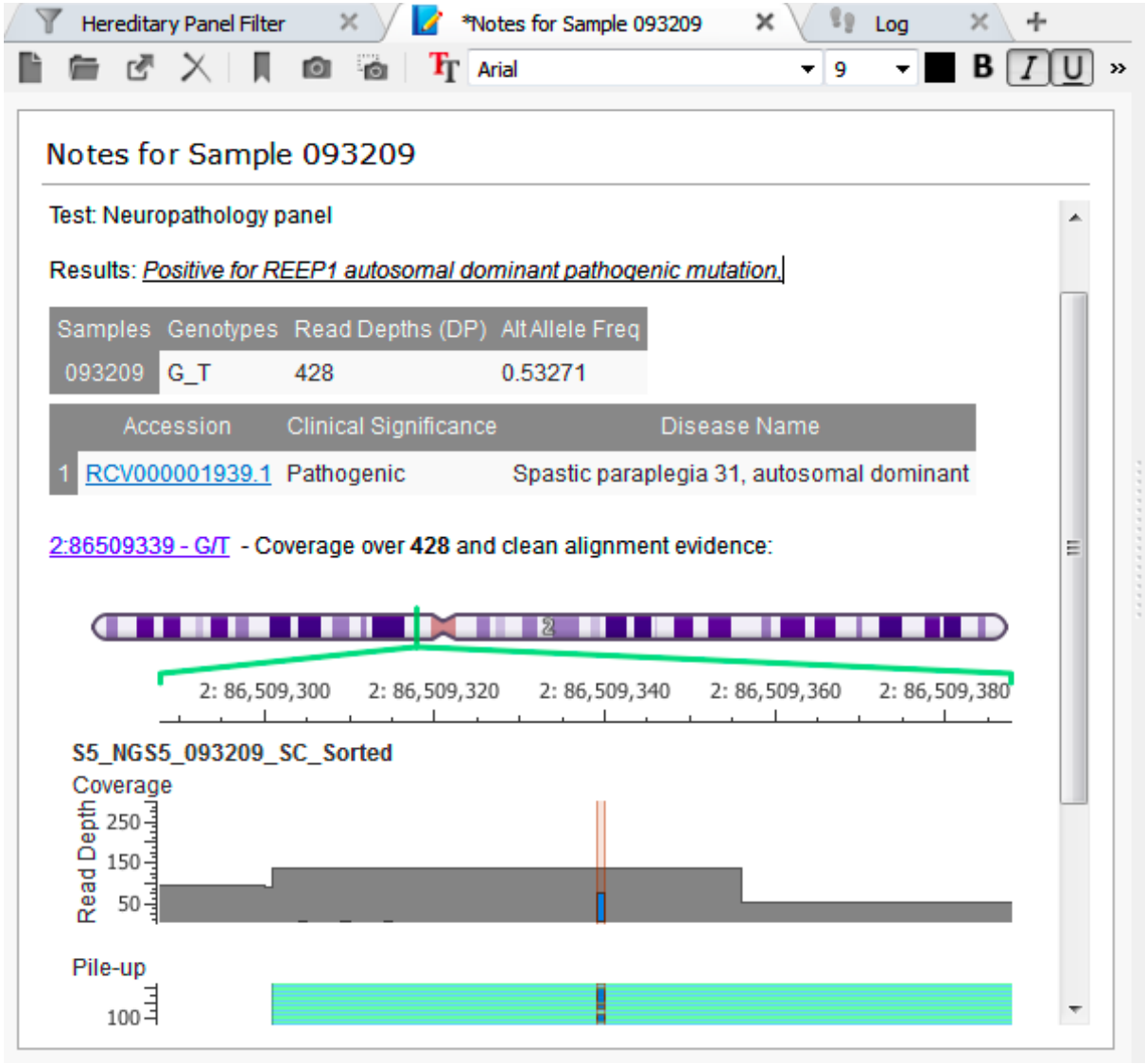
3. **Knowledge Capture: Leveraging Insights**
4. Prioritize: Best Candidates First

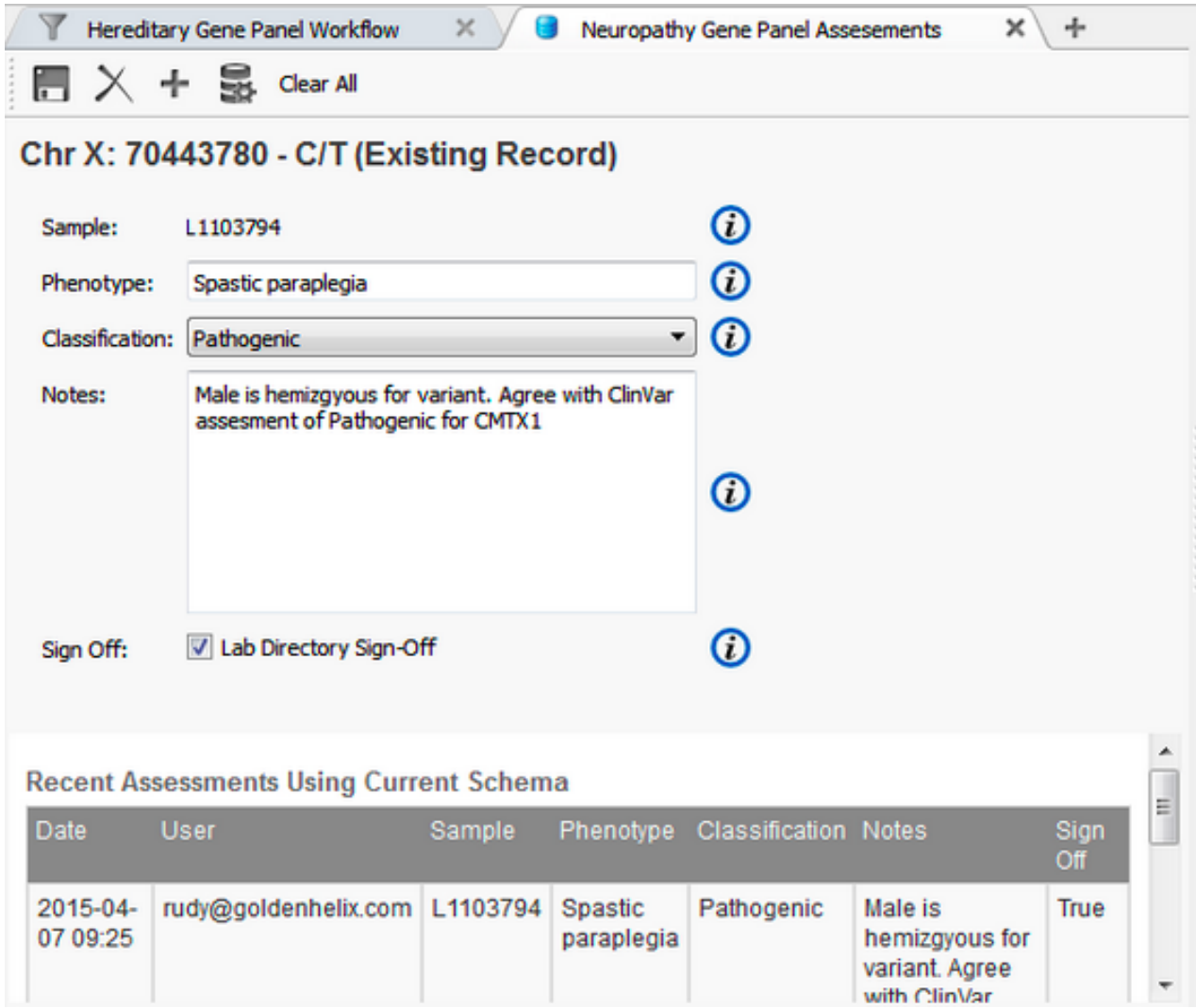
Knowledge Capture - Project Notes

- **Rich text edit controls**
- **Save as HTML, PDF**
- **Grab content from:**
  - Details view
  - Table
  - GenomeBrowse view
- **Saved with project**
- **Multiple per project**



Knowledge Capture – Variant Database

- **Customizable set of fields and defaults**
- **Use for annotation**
- **Backends:**
  - Single file (SQLite)
  - MySQL
  - PostgreSQL
- **Fully logged**
- **Revertible**
- **Auto-fields:**
  - Sample
  - Project



[Demonstration]

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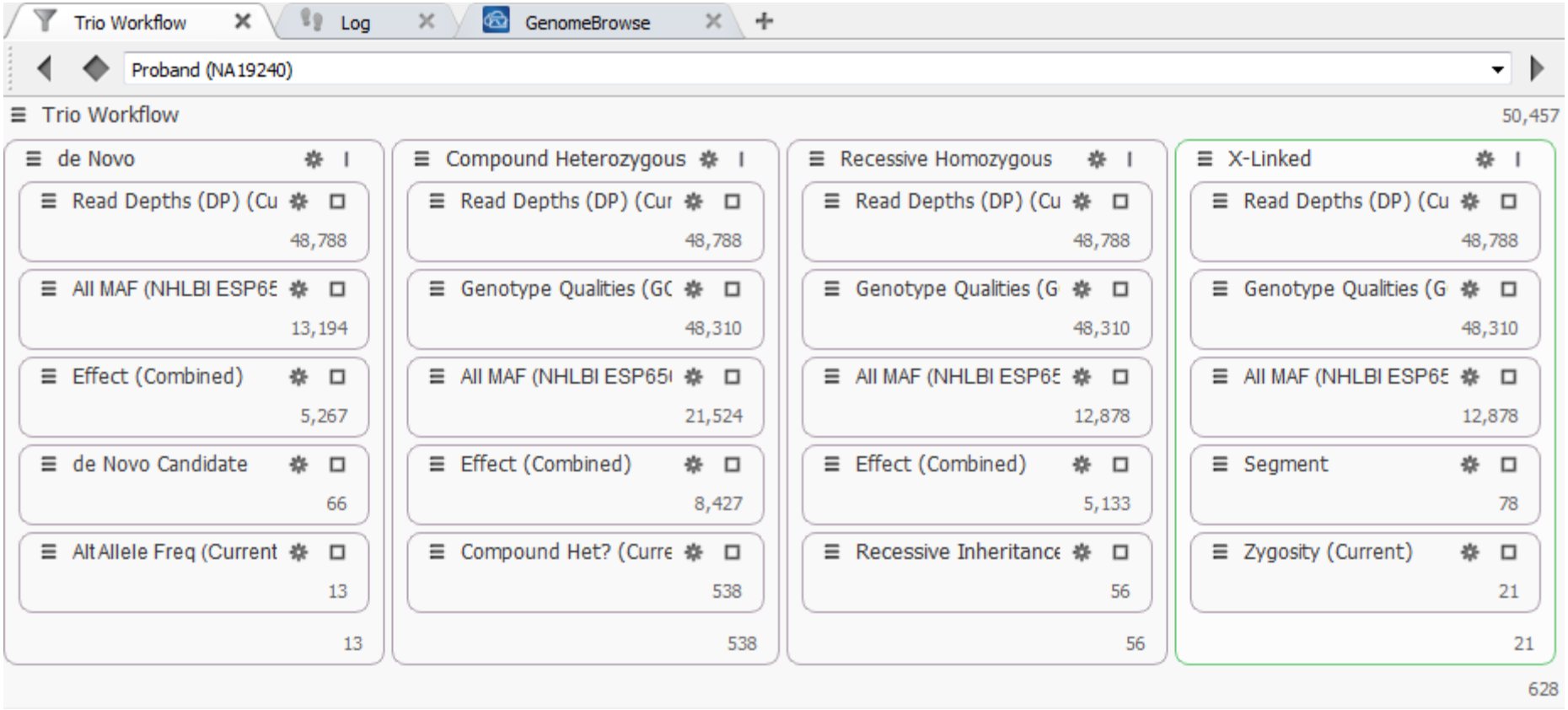
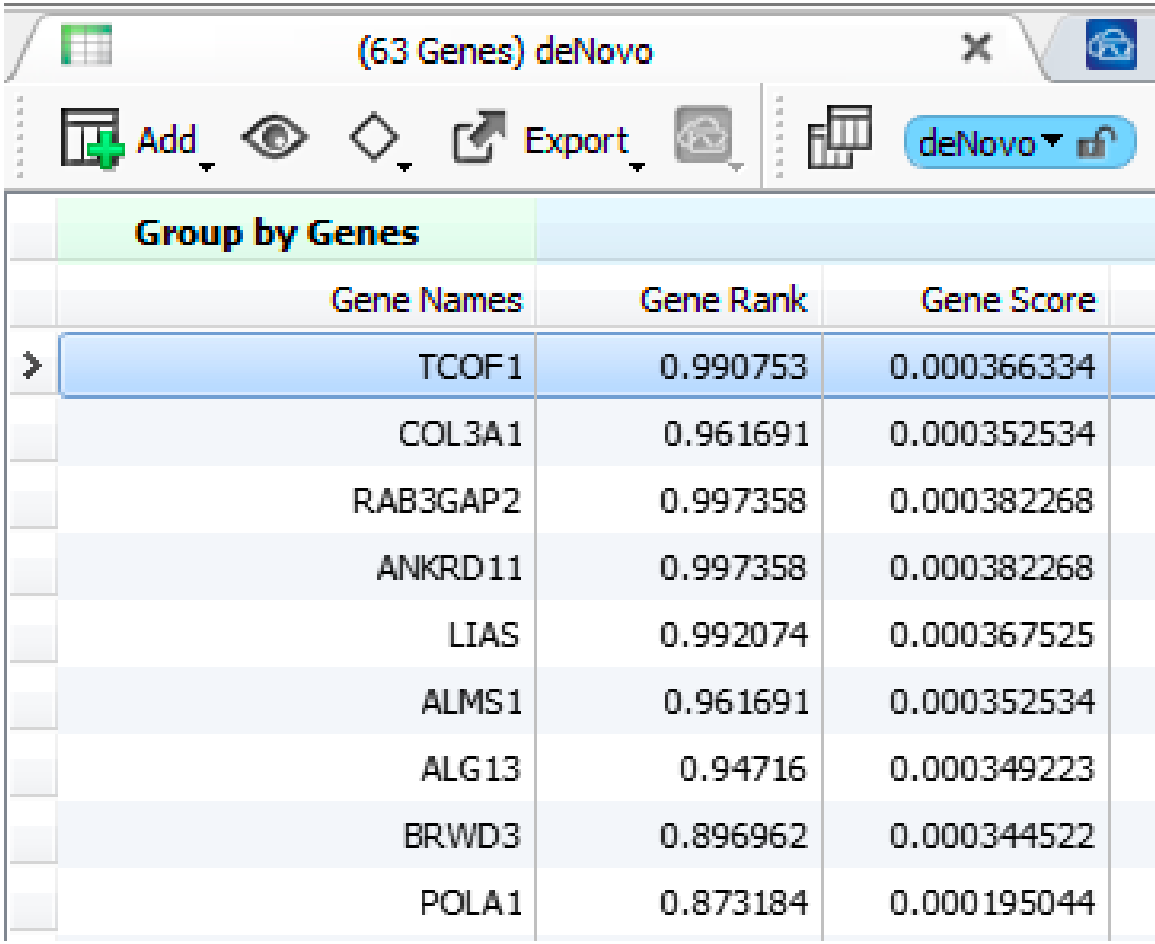
Annotate, Filter and Rank



PhoRank – Phenotype Based Gene Ranking

- Sorting and Ranking harmonized
- Enter phenotype terms using HPO
- Propagates terms through HPO and GO
- Ranks genes in dataset by known associations with terms
- Provides path back to input terms



Group by Genes

Gene Names	Gene Rank	Gene Score
TCOF1	0.990753	0.000366334
COL3A1	0.961691	0.000352534
RAB3GAP2	0.997358	0.000382268
ANKRD11	0.997358	0.000382268
LIAS	0.992074	0.000367525
ALMS1	0.961691	0.000352534
ALG13	0.94716	0.000349223
BRWD3	0.896962	0.000344522
POLA1	0.873184	0.000195044

[Demonstration]

VarSeq

- Enables repeatable processes
- Supports clinical lab requirements
- Gene panels, exomes
- Simple and intuitive interface
- Fast and responsive
- Simple licensing model

Questions or more info:

- Email info@goldenhelix.com
- Request an evaluation of the software at www.goldenhelix.com

Questions?

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