Overview of QIAGEN Bioinformatics Products and Solutions

Michael Hansen Ph.D. Technical Application Specialist
Author: Tim Bonnert, Ph.D. Associate Director, Field Application Scientists, EMEA
QIAGEN Sample to Insight

Sample Isolation
- QIAamp DNA Kits
- PAXgene RNA/DNA Kits
- GeneRead DNA FFPE Kit
- QIAamp Circulating NA Kit
- exoRNeasy Kits
- RNeasy Kits

Targeted Enrichment
- QIAseq Targeted RNA Panels
- QIAseq DNAseq Panels

Library Construction
- QIAseq FX Library Kits
- QIAseq 1-step Amplicon Kit
- QIAseq Ultralow Input Kit
- REPLI-g® Single Cell Kits

NGS Run
- Ion Torrent
- Illumina

Data Analysis
- Biomedical Genomics Workbench
- Genomics Server Solution
- CLC Genomics Workbench
- Microbial Genomics Pro Suite
- QIAGEN® Clinical Insight Analyze
- OmicSoft Array Suite

Integration
- Ingenuity Variant Analysis
- QIAGEN® Clinical Insight Interpret
- Ingenuity Pathway Analysis
- HGMD®
- Inova Genomes
- OmicSoft Lands: DiseaseLand OncoLand GeneticsLand

Sample to Insight
Streamlined workflows and a rich toolbox to efficiently process data
Comprehensive biological insights

**Upstream Analysis**
- Functions
  - Networks
  - Mechanistic Networks
  - Canonical Pathways
  - Lipoprotein metabolism

**Sample to Insight**
IPA with Analysis Match: The Power to Discover

- **Causal Network Analysis**
  - Predict regulatory networks responsible for observed expression changes

- **BioProfiler**
  - Identify molecules causally relevant to phenotype of interest

- **Relationship Export**
  - Export molecules and relationships from a network or pathway

- **IsoProfiler**
  - Identify biologically significant isoforms in your dataset

- **Phosphorylation Analysis**
  - Predict impact of phospho proteins on Canonical Pathways and functions. Find upstream regulator drivers

- **Analysis Match**
  - Discover other IPA Core Analyses with similar (or opposite) biological results by comparing to over 6,500 analyses of data from OmicSoft DiseaseLand and OncoLand
Integration of tools into single NGS analysis platform

Microbiome Profiling
- Function
- Taxonomy

NGS-based typing
- Taxonomy
- AM resistance
- Epidemiology

Genome/Metagenome Assembly
- De novo assembly (+PacBio)
- Gene finding, Annotation

+ 3rd party extensibility
(CosmosID GeneProbe Inc.)
Intestinal Flora Diversity Testing for FMT in the Clinic

• Obtain measure of species diversity in the intestinal flora by analysis of the 16S gene
• Predict the benefit of fecal microbiota transplant (FMT) through patient and donor analyses
• Patients with C. difficile infection have severe diarrhea
• Very difficult to treat with antibiotics 10-20% effective
• In contrast, 80-90% can be cured with FMT
• Future use for more diseases? (autoimmunity, psychosomatic…)
HGMD® is the industry standard for inherited disease mutations

- Identify known genetic causes of an inherited disease
- Understand the mutational spectrum of a gene
- Verify novel mutations
- Assess individual disease risk
- Reducing time for literature review relating to a given inherited disease

### Winter 2017 Release Statistics

<table>
<thead>
<tr>
<th>Mutation type</th>
<th>Total number of entries for release 2017.4</th>
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<tbody>
<tr>
<td>Missense/nonsense</td>
<td>124511 (5771)</td>
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<tr>
<td>Splicing</td>
<td>19796 (655)</td>
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<td>Regulatory</td>
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<tr>
<td>Small deletions</td>
<td>32440 (314)</td>
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<tr>
<td>Small insertions</td>
<td>13570 (195)</td>
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<tr>
<td>Small indels</td>
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<tr>
<td>Repeat variations</td>
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<tr>
<td>Gross insertions/duplications</td>
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<tr>
<td>Complex rearrangements</td>
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<tr>
<td>Gross deletions</td>
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<td><strong>Total</strong></td>
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<table>
<thead>
<tr>
<th>Variant class</th>
<th>Total number of entries for release 2017.4</th>
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<tbody>
<tr>
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<td>DM?</td>
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<td>R</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>220270</strong></td>
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</table>
A day trip to London…

…An information, integration and analytics challenge

- Aggregation is not Integration
- Integrated content is greater than the sum of its parts

- Multiple content sources
- Integration of content
- Context-relevant analytics
The Most Comprehensive Knowledge Base for ‘Oomics Interpretation

### Variant Analysis and Prioritization

<table>
<thead>
<tr>
<th>QIAGEN Clinical Insight</th>
<th>Expression &amp; Pathway Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variant Analysis</strong></td>
<td><strong>Expression &amp; Pathway Analysis</strong></td>
</tr>
<tr>
<td>Encode</td>
<td>TCGA</td>
</tr>
<tr>
<td>ClinVar</td>
<td>GEO, Array Express</td>
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<tr>
<td>Public Frequency Databases</td>
<td>GTEx</td>
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<tr>
<td>Jaspar</td>
<td>ICGC</td>
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<tr>
<td>Pathways &amp; Path to Phenotype</td>
<td>TARGET, BLUE-PRINT</td>
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<td>Inova Genome Compendium</td>
<td>NCI, SRA, dbGAP</td>
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<tr>
<td>Rapid Release Bibliography</td>
<td>PGMD PGx</td>
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<td>PGMD PGx</td>
<td>Cardiovascular, Metabolic, Neuro, Immuno Datasets</td>
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<tr>
<td>Allele Frequency Community</td>
<td>Clinical Trials</td>
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<tr>
<td>HGMD Pro</td>
<td>Clinical Trials</td>
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<tr>
<td>Curated Somatic Variants</td>
<td>Drug Labels</td>
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<td>Deep Curated Disease Variants</td>
<td>Clinical Case Counts</td>
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<tr>
<td>Curated Guidelines</td>
<td>TCGA</td>
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</tbody>
</table>

### Content

- **Public Database Modeled/Structured by QIAGEN**
- **Licensed Database Modeled/Structured by QIAGEN**
- **Content Curated/Exclusively Distributed by QIAGEN**
The QIAGEN Knowledge Base: Content & Content-aware Analytics

- Cancer Scoring
- Hereditary Disease Scoring
- Causal Network Analysis
- Drugable Pathways
- Disease Model-based Analysis
QIAact panels based on leading QIAGEN Knowledge Base

QIAGEN Knowledge Base
- Industry-leading, comprehensive database
- Compilation of multiple public and proprietary sources
- Expertly curated and continuously updated

The design of GeneReader QIAact panels are based on:
- Drug labels
- Clinical trials
- Professional guidelines

Panel designs to deliver clinically relevant insights
QIAGEN Clinical Insight: The Bioinformatics QIAGEN’s NGS System

- Algorithms
- Optimized Workflows
- Knowledge bases
- Ontology

Sample to Insight
QIAGEN is the world’s largest Bioinformatics company!

Primary analysis (Base calling)

- Raw data
- FASTQ file generated by any NGS platform

Secondary analysis (Alignment and variant calling)

- QIAGEN’s
  - Genomics Workbench
  - Clinical Genomics Workbench
  - QCI Analysis

- Easy-to-use flexible & scalable bioinformatics solution
- “Any and every” tool for bioinformatic analyses
- Graphical User Interface
- Highly automated software

Tertiary analysis (Biological interpretation)

- QIAGEN’s
  - Pathway Analysis
  - Variant Analysis
  - QCI Interpretation

- Finding causative variants fast with up-to-date scientific knowledge
  - Curated biological knowledge and databases
  - Annotate & filter variants
  - Link variants to biology
  - Link variants to treatments & trials
What it is:
- Evidence-based software that assists you in scaling your NGS DNA test interpretation and reporting capabilities
- Comprehensive annotation and bibliographic literature reference support
- Customizable rules-based reporting
- Relevant up-to-date treatment and clinical trial information
- Standardized platform converts manual variant research to clickable reviews

What it Enables:
- Reduce the time, cost, and complexities associated with NGS tests
- Improve ability to determine disease causing and actionable variants
- Increase treatment and clinical-trial matching
- Private, experiential database grows with each variant assessed and reported
- Enabler of training and results communication
Biological Interpretation of Causal Variants

Biological interpretation of human whole genome, exome, and targeted panel samples

- Sequence and align
- Generate called variants file
- Upload samples
- Combine into analyses
- Annotate and interactively filter
- Share and publish samples and analyses

- Gene A
- Gene B
- Gene C
- Disease

Scalable Workflows
- Stratification Studies
- Large Cancer Studies
- Genetic Disease Cohort
- Trio/Quad Study
- Tumour-Normal Pair
- Personal Genome

Pedigree Support
- Disease Identification
- Statistical Burden Testing
DNA-Seq controlled workflow

**Interpretation – Qiagen Clinical Insight Interpret**

- Platform agnostic web-based application for interpretation and reporting of variants
- A knowledge-based decision support tool
- Standardizes, simplifies and speeds-up the process of classifying variants

✓ Applies the ACMG Guidelines for variant classification
✓ Optimized for somatic and hereditary cancer
✓ Associates variants with relevant up-to-date treatment and clinical trial information
✓ Standardized assessment platform which removes the need for manual variant research
✓ Allows the development of an in-house database of classified and reported variants
The goal of clinical pathology:

- A clear report on the pathogenic or actionable variants in the sample and the treatments, trials and evidence for that assessment.

Too often, the reality:

- Complex pipelines of scripting and file conversion, different tables of variants, searching across multiple content sources, inefficient identification of supporting evidence and publications.
Most actionable panel for first-line testing

**Actionable Tumor Insight Panel**

Targeting solid tumors with:
- Highest prevalence
- Greatest need for testing
- Variants associated with actionable insights

12 genes for mutation analysis:
- KRAS
- NRAS
- KIT
- BRAF
- PDGFRA
- ALK
- EGFR
- ERBB2
- PIK3CA
- ERBB3
- ESR1
- RAF1
Same genes, **NOT** the Same Insights

<table>
<thead>
<tr>
<th>Genes</th>
<th>Not covered by Thermo AmpliSeq HotSpot Panel V2</th>
<th>Not covered by Illumina TruSight Tumor 26 Panel</th>
<th>Not covered by either</th>
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<tbody>
<tr>
<td>EGFR</td>
<td>58</td>
<td>28</td>
<td>21</td>
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<tr>
<td>PI3KCA</td>
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<td>KIT</td>
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<td>KRAS</td>
<td>12</td>
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<td>BRAF</td>
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<td>ERBB2</td>
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<tr>
<td>PDGFRA</td>
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<td>5</td>
<td>4</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>181</strong></td>
<td><strong>117</strong></td>
<td><strong>81</strong></td>
</tr>
</tbody>
</table>
• Variant list screen shows overview of validated variants
  • Colour coded classification of variants
  • Complete transparency of classification evidence
  • Actionable variants highlighted
Flexible Treatment Information

- See approved drugs from EMA, FDA, ESMO, ASCO and NCCN (configurable)
- See clinical trials specific to geographical location
QIAact panel portfolio: maximum actionability within 30 days

- **Actionable Insights**
  - Tumor Panel (FFPE 5%, LB 1%)

- **BRCA 1/2 Panel** (FFPE/Blood) (somatic 5%, germline)
- **Lung All-in-One DNA & Fusions Panel** (FFPE 5% / LB 1%)
- **Myeloid Leukemia Panel** (July 2018)
- **BRCA extension** (p53, pTen) (June 2018)
- **Custom Panels** (FFPE/LB/Blood)

Based on QIAGEN knowledge base, enabling maximum actionability
Verified performance from sample to insight workflows, enabling any lab to go live within 30 days
QIAact custom panels: maximum actionability within 30 days

- BRCA 1/2 Panel
- Lung All-in-One DNA & Fusions Panel
- Myeloid Leukemia Panel (Q2 2018)
- BRCA extension (p53, pTen) (Q1 2018)
- Custom Panels (FFPE/LB/blood) (examples Feb 2018)
  - Lymphoma
  - Neuropathology
  - Glioblastoma
  - Endometriotic cancer
  - CFTR
  - Hypercholesterolemia
  - Thrombosis
  - HID (Missing Persons, paternity, ancestry, phenotypic, mitochondrial WG)
  - Etc. …

Optimized panel designs and Bfx workflows based on customer demands
Guaranteed coverage from sample to insight workflow, verification of performance made by customer
QIAact Myeloid Leukemia panel (MLP) incl. 25 genes

Available July 2018

Molecular screening of myeloid neoplasms for somatic DNA mutations
Target examples: JAK2, CALR, MPL, ASXL1, IDH1/2, TET2, DNMT3A,…
QCI Interpret is an evidence-based decision support software intended as an aid in the interpretation of variants observed in genomic next-generation sequencing data. The software evaluates genomic variants in the context of published biomedical literature, professional association guidelines, publicly available databases, annotations, drug labels, and clinical-trials. Based on this evaluation, the software proposes a classification and bibliographic references to aid in the interpretation of observed variants. The software is NOT intended as a primary diagnostic tool by physicians or to be used as a substitute for professional healthcare advice. Each laboratory is responsible for ensuring compliance with applicable international, national, and local clinical laboratory regulations and other specific accreditations requirements.

For up-to-date licensing information and product-specific disclaimers, see the respective QIAGEN kit handbook or user manual. QIAGEN kit handbooks and user manuals are available at www.qiagen.com or can be requested from QIAGEN Technical Services or your local distributor.

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