Quest Diagnostics
Genetics and DNA combing

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Outline

- Quest Diagnostics overview – Empowering Better Health With Diagnostic Insights
- Genetics at Quest
- Quest Genetics Programs and DNA Combing / GV
Delivery of proven care to the right patients and populations is very difficult in our complex and changing healthcare system.
Quest is a major player in healthcare…

- Serves 50% of hospitals
- Access to ~80% of U.S. insured lives
- 470,000 Physicians connected to Care360 portal
- Serves 1/3 of the U.S. adult population and ~50% within 3 years
- 675+ EMR interfaces
- Expanding retail presence
- Q² Solutions helped develop 50% of all FDA-approved Oncology Precision Medicine drugs since 2014
- 470,000 Physicians connected to Care360 portal
- Access to ~80% of U.S. insured lives
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Quest Diagnostics is enabling better and more cost-effective care across our healthcare system

- Partnerships with leaders in healthcare
- Application of big data to improve population health
- Smart use of HIT tools and integrated solutions
- Hospital to Home: right care, right cost, in a convenient way
- Enabling consumers to access care and improve health
- Leading in delivering advanced diagnostics to the community

Empowering better health with diagnostic insights
Technology continues to deliver clinical value and we have delivered many industry firsts.

| **Personalized Medicine** | OncoVantage™ IBM Watson Genomics from Quest  
|                          | Companion development & commercialization (Biogen /JCV, Pfizer / HIV tropism, BMS/PDL1) |
| **Cancer predisposition- Qvantage** | Created collaborative BRCAsave database with INSERM  
|                          | Launched Qvantage 34 gene panel |
| **Reproductive Genetics** | Non-invasive prenatal testing solution Qnatal  
|                          | First High-throughput Fragile X assay  
|                          | Cystic Fibrosis by NGS |
| **Neurology** | World-leading database for genetics and immunology in neurology  
|                          | **First DNA combing test in US - FSHD**  
|                          | Integrated pathway solutions: genetics, phenotyping, cognitive testing and imaging |
| **Infectious Diseases** | First Lab in US to offer testing for H1N1, Chikungunya and Zika  
|                          | Developed HIV tropism by NGS – included in guidelines |
| **Mass spectrometry** | Many industry firsts – thyrogblobulin, comprehensive steroids, insulin, renin |
| **Sampling technologies** | Largest provider of finger-stick based testing in the world (~1.5M / year)  
|                          | Proprietary approach to finger-stick testing for the vast majority of our menu |
Quanum: A critical enabler of solutions for populations, providers and patients
Our data — driving value for our customers and country

- HCV screening and treatment with CDC
- Closing gaps in care with Data Diagnostics®
- Diabetes prevention with AMA and CDC
- Improving clinical trials enrollment with pharma and academia
- Improving BRCA mutation analysis with BRCA Share™
- PDM Health Trends™ report
- Access to cancer precision medicine with IBM Watson and MSKCC
We support diagnostic information services across healthcare

**General Diagnostics**
- Cardiometabolic & Endocrine
- Prescription Drug Monitoring
- Infectious Diseases & Immunology

**Advanced Diagnostics**
- Cancer Diagnostics
- Women’s Health
- Neurology

**Diagnostic Services**
- Professional Lab Services
- Employer and Consumer
- Clinical Trials / Q2 Solutions
- Sports Diagnostics
Leading in advanced diagnostics—delivering high clinical value to the medical community across the U.S.

- Neurology genetics and advanced biomarkers
- Cancer genomics
- Non-invasive prenatal testing
- Mosquito borne infection (Zika)

Quest is the market leader in Advanced Diagnostics
We are delivering healthcare at the right time, in the right place, at the right cost, in a more convenient way.

Hospital to Home: Quest Extended Care Services

Self-collection / minimally invasive technology

>7000 mobile phlebotomists and NPs

Virtual Clinic and In-Home Medical Diagnostics –

EKG; Spirometry
Ultrasound
Eye exam; ENT exam

Safeway
MyQuest by Care360
Teladoc

Quest Diagnostics
Quest and Q² Solutions are enabling all aspects of drug and companion development

Integrated CDx Solutions with

Marker selection & study design, Informatics/Analytics

Assay development, validation & scale up

Strategic consulting: regulatory & reimbursement, Enrollment Solutions

Global clinical trial wraparound services including Central Lab

Deep experience in 3-4 way CDx development relationships

Registration & market access expertise (510(k); PMA; CE Mark)

Access to Reagent kit production / GMP

Pre-launch medical communications & proficiency training

Commercial, diagnostic & market analytics capabilities

Rx  | Preclinical | Clinical Development | FDA Filing | Launch
---|-------------|----------------------|------------|-----
IVD | Feasibility | Development          | Lab Validation | Clinical Validation | IVD Registration | Commercialization & Modification

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We have built a global clinical trials and clinical laboratory network
Genetic Testing at Quest Diagnostics

Overview, FSHD, SMA
Responsible Genomics

- Testing driven by clinical presentation, algorithmic efficiency and economy
- Access and consultation with board-certified geneticists, genetic counselors, doctors, scientists, and researchers
- Patient financial assistance programs and affordable test pricing
- Collaboration: Sharing our explorations of the genetic frontier to promote discovery and insight
Comprehensive and responsible testing

A technology-agnostic approach to diagnosis

- Confirm a specific genetic syndrome
- Establish the genetic cause of disorder
- Provide information about prognosis
- Selection of treatment options
- Predictive testing for asymptomatic family members
- Genetic counseling for recurrence risk determination and family planning
We offer 750+ genetic tests

- Experience with Unusual and Rare Cases
- Innovative Test Menu that Spans Across All Areas
- Clinically Appropriate Testing
- Continuum of Care
Examples of Genetic/Genomic Test Offerings

Women’s and Reproductive Health
- Carrier screen – Cystic Fibrosis, SMA, Fragile X
- Hemoglobinopathies
- Panethnic Carrier Screen (QHerit)
- NIPS (Qnatal) + microdeletions

Oncology
- Hereditary Cancer panels (BRCA1/2, Myvantage (34 genes), Givantage (13 genes), JPS, PJS, Lynch syndrome, single genes)
- Solid tumor – OncoVantage50,
- Hemepath - Leukovantage
- Thyroid cancer

Neurology, Renal, Endocrine
- Mendelian disorders – Fragile X, SMA, others
- Epilepsy, muscular dystrophy, developmental delay/intellectual disability, cerebrovascular, dementia, neurodegenerative disorders, neuromuscular, neuronal, hearing loss, mitochondrial disorders, others
- Neurome (Whole Exome Sequencing)
- Inherited renal disorders
- Endocrine disorders - inborn errors of metabolism
Fascioscapulohumeral muscular dystrophy

• FSH Muscular Dystrophy (FSHD) results in a life-long, progressive loss of skeletal muscle: face, arms, shoulders, back and legs, core and beyond.

• It is caused by contraction of a microsatellite (D4Z4 repeat, 3.3\kb/unit)

• An estimated 870,000 people worldwide have FSHD.

• Symptoms may be evident at birth or during childhood, but more often appear during teenage and adult years.

• FSHD can be profoundly disabling, causing a loss of facial expression, difficulties with speech and hearing, and inability to lift objects or walk.

• There is no effective treatment or cure.
Spinal muscular atrophy (SMA)

- Autosomal recessive
- Most common genetic cause of infant and childhood mortality
- Degenerative disease leading to atrophy and weakness
- Incidence – 1:6,000-10,000 live births
- Pan-ethnic carrier frequency – 1:54
- A component of a very large testing segment for Quest Diagnostics - carrier screening and reproductive genetics
  - CF, Fragile X, SMA, AJP, NIPT


# Genetic testing: carrier

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<tr>
<th>Interpretation</th>
<th>Results</th>
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| Normal         | 2 copies of *SMN1*  
|                | • Residual risk of being carrier (e.g. 2+0)  
|                | • 4% of 2 copy carriers are 2+0 |
| Carrier        | One copy of *SMN1*  
|                | • ¼ chance of having an affected child  
|                | • Partners should be tested  
|                | • Prenatal/Postnatal testing should be discussed |
| Affected       | 0 copies of *SMN1*  
|                | Several copies of *SMN2* |
Autosomal recessive inheritance with high carrier frequency in the general population

Phenotype-genotype correlation can be complex
- Modifiers, e.g. SMN2 copy number, point mutations in SMN2, epigenetics
- Classification categories are aggregates of phenotypes

Carrier results have some limitations
- Residual risks for 2+0 and 3+0 SMN1 carriers -> opportunity for DNA combing to define carrier testing
- De novo risk

Current technology has limitations
- Sequencing cannot differentiate SMN1 v SMN2 in carriers
- Atypical results

Diagnostic testing availability
- PGD (requires proband), Prenatal (CVS, Amniocentesis), Cord blood, Postnatal
Quest Genetics and DNA combing - summary
Quest and Genomic Vision

- Quest and GV have had a strong collaboration for the last 5+ years and are working very closely today on development of applications for DNA combing.

- DNA combing enables detection of complex genetic rearrangements which are not detected with traditional genetic testing technologies.

- Quest is investing aggressively in genetics and is collaborating with Genomic Vision to enhance our services.

- We believe DNA Combing can enable enhanced value by enabling detection of clinically relevant genomic changes which are missed by all current technologies and testing services in the market.

- Quest is working with GV to develop genetic testing content enabled by DNA combing across several areas and leveraging our clinical samples, relationships and expertise.

- DNA combing may be used as a clinical testing technology or as a discovery tool to enable enhancement of genetic testing using PCR and Sequencing techniques.
# Quest and Genomic Vision

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<th>Genetic testing segment</th>
<th>DNA Combing application / program</th>
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| FSHD – Genetic Syndromes                    | ✓ FSHD improves sensitivity of testing vs. Southern  
✓ Combing is the preferred FSHD method for Quest  
✓ Converting clients to this technology and implementing in Marlboro Lab (Athena)  
✓ Evaluating additional genetic syndromes for applicability |
| Cancer Genetic Predisposition                | ✓ BRCA market has moved to broader gene panels (Quest MyVantage 34 Genes)  
✓ BRCA still the most important genes and differentiation in the market is needed  
✓ HNPCC testing - MSH2 Inversion characterized by DNA combing can be implemented using sequencing and PCR  
✓ GV analyzing data for BRCA and HNPCC from collaborative studies using Quest samples to enable Quest assay development based on results |
| SMA 2+0                                      | ✓ Significant value in enabling testing for SMA “2+0” carrier status  
✓ GV mapping SMA and Quest + GV collaborating to enable development of testing for 2+0                                                                 |
| Pharmaceutical services                     | ✓ DNA combing can be used as a unique biomarker tool for drug development for gene therapy and editing and DNA replication inhibitor applications  
✓ DNA combing to be made available to clients of Q2 Solutions |
| Research database                            | ✓ Potential for GV to develop a broad genetics database characterizing DNA rearrangements across diseases areas in collaboration with researchers around the world  
✓ Data might inform on genetic testing services application design and life-cycle |

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[Quest Diagnostics](https://www.questdiagnostics.com)