Eugene Consulting Inc.
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August/September 2020 Report

Gene By Gene (https://genebygene.com)

- A commercial genetic testing company based in Houston, Texas
  - Specializes in DNA-based ancestry and genealogy
  - The world's first company to develop consumer DNA testing products for ancestry and genealogy applications
- Founded in 2000
- Founders: Bennett Greenspan (https://www.linkedin.com/in/bennett-greenspan-1a43676) and Max Blankfeld (https://www.linkedin.com/in/max-blankfeld-80b3623/)
- Subsidiaries:
  - Family Tree DNA - https://www.familytreedna.com/
  - Arpeggi Inc.
    - On July 13, 2013, Gene by Gene Acquired Arpeggi, a Startup health and GE-backed company that develops solutions for genome sequencing, data management and computational analysis
    - The acquisition of the company will support Gene and Gene achieve its goals of making next-generation DNA sequencing and clinical genomics accessible and affordable to all
    - Arpeggi was founded in 2012 and in April of 2013, they release GCAT, Genome Comparison And Analytic Testing, which is a free community driven platform for evaluating the performance of next-generation sequencing data analysis methods
    - The entire Arpeggi team and technology platform has been incorporated into Gene by Gene
    - Arpeggi's founders also joined Gene by Gene's management team
- Raised 1 seed round of funding –for an undisclosed amount – on July 18, 2013
  - Funded by Startup Health

Products

- Customers are provided buccal (cheek) swab kits with each order
  - Each test requires 2 buccal swabs
  - Each kit comes with return packaging and pre-paid shipping label
- *Whole Exome Sequencing*
  - Exome sequencing has the ability to simultaneously analyse approximately 60 million base pairs, representing 22,000 genes using next-generation sequencing
  - This can help identify variants that may be the genetic cause of a wide range of traits and conditions
  - Platform: Illumina HiSeq

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    - Result Delivery: Results are delivered to the customer via electronic FTP transfer and are only stored by Gene By Gene for 30 days
- *Whole Genome Sequencing*
    - Offers a high degree of accuracy in identifying variants across the entire scope of the human genome
    - Can only be completed with a blood sample
    - Platform: Illumina HiSeq
- *Complete Mitochondrial Sequencing (mtDNA)* –
    - *H*ighest level of mtDNA testing available
    - Covers all 16,659 base pairs which includes HVR1 and HVR2 regions, and the coding region
    - Test also includes alignment and variant calling analytics
    - Platform: Illumina MiSeq
    - Result Delivery: Results will be available for customer via electronic FTP transfer and are only stored by Gene By Gene for 30-60 days
- *Fragile X* –
    - To examine carrier status of Fragile X syndrome
    - CGG repeat size is assessed using AmplideX FMR1
    - Results are reported in reference to Human Genome 19, Human Build 37
    - Methodology:
        - Once DNA is extracted, it is amplified to obtain coding exons and their flanking regions
        - Sanger-sequencing method is used and all fragments are sequenced by forward and reverse internal primers when possible to determine the noted regions
        - When this is not possible, PCR and sequencing are performed in at least 2 independent reactions in 1 direction
        - Mutations are scored relative to reference sequencing in the publicly available database NCBI and following the recommendations of the human genetic variation nomenclature scheme
        - Exome 1 of the tested gene is defined as the exon in which the first ATG appears
        - Chromosomal positions are indicated according to the hg19 reference assembly
        - Reports are reviewed and approved by the Gene by Gene Chief Medical Officer and the Clinical Laboratory Director
- *Illumina Global Screening Array* –
    - Optimized tag SNP content from all 3 HapMap phases has been strategically selected to capture the greatest amount of common variation and drive the discovery of novel associations with traits and conditions

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    - The Infinium Global Screening Array-24 v2.0 BeadChip combines multi-ethnic genome-wide content, curated clinical research variants, and quality control (QC) markers for precision medicine research.
    - Samples are analyzed using the Illumina HumanOmniExpress BeadChip process and genome build GRCh37/hg19
    - All data collected is evaluated using Illumina's GenomeStudio v2.0 software
    - Genotypes obtained from the Illumina Global Screening Array can be used to identify copy number variations (CNVs)
- *Sanger Sequencing* – includes full sequencing of the exons in the associated gene, +/- 10bp into the flanking intronic regions
    - Used to look at the entire sequencing of a gene to identify potential variations
    - A clinical genetic test that delivers information on any variants and their clinical significance
    - Follows the same methodology as the *Fragile X* test
- *SARS-CoV-2 Detection Test*
    - Detects the presence of nucleic acid from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) that causes novel coronavirus disease (COVID-19)
    - Intended use is for patients who meet the Centers for Disease Control and Prevention (CDC) criteria for evaluation of infection with COVID-19.
    - a real-time RT-PCR (rRT-PCR) assay used to detect the presence of SARS-CoV-2 RNA isolated from respiratory specimens.
    - Following receiving swab specimens, nucleic acid will be extracted using an automated system followed by an rRT-PCR assay.
    - A nasal swab kit will be provided with each order
    - Samples must be collected by a qualified healthcare professional
- *Tryptase CNV Testing (Genetic Copy Number Variation Test)*
    - For patients who exhibit any of the following symptoms:
        - A tryptase level of 6 or more
        - Cutaneous flushing, itching, and severe allergic reactions
        - Dysautonomia
        - Chronic pain
        - Connective tissue abnormalities
    - For patients who have been diagnosed with any of the following
        - Mast Cell Activation Syndrome (MCAS)
        - Postural Orthostatic Tachycardia Syndrome
        - Gastroparesis
        - Ehlers-Danlos Syndrome
    - Test may be self-administered– during an office visit or at home
    - Can access and download the results online

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Services

- FamilyTreeDNA -a direct-to-consumer DNA testing company for ancestry
    - Family ancestry kit – $70 USD
        - Discover ethnic and geographic origins
        - Find unknown realtives
        - ancientOrigina (latest enhancement to Family Finder) allows you to compare your DNA to DNA from archeological dig sites throughout the European continent
        - can find out how much autosomal DNA you still carry of the ancient European groups
        - can explore ancient ancestors migration routes
        - Users can only view, sort, and compare DNA matches by parental lines
    - Paternal Ancestry (male-specific test) - $119 USD
        - Uses males Y-DNA to determine where their direct paternal ancestors came from and how they migrated
        - There are 3 test: one that examines 37 short tandem repeats on the Y-chromosome, another than examines 111 and a third that examines 700 short tandem repeats and over 200k SNPs on the Y chromosome
    - Maternal Ancestry
        - Trace maternal ancestry using advanced mtDNA tests and the world' largest mtDNA database
        - Use mtDNA to determine where their direct maternal ancestors came from and how they migrated
        - New feature: mtFull Sequence video
            - Tells the story of your maternal ancestry and is a fun way to share results with others
- Carrier Screening
    - Provides customers with information on their risk of having a baby with a genetic condition
    - Tests for 253 autosomal recessive and X-linked recessive conditions
    - List of conditions tested: https://genebygene.com/wp-content/uploads/2019/08/GeneByGene-Carrier-Screen-Conditions.pdf
    - Sample collection is done with a cheek swab
    - Results are laid out in a simple report – 1st page = summers, follow pages provide details
    - Sample report: https://genebygene.com/wp-content/uploads/2019/08/sample-report.pdf
    - Screening Process

        1) Patient and healthcare provider make the decision to order genetic carrier screening

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2) Sample collection using a check swab
3) Sample is sent to Gene by Gene's lab
4) Results are provided in 2 weeks after sample is received
5) If results indicate you are a carrier for a condition tested, a meeting with a genetic counselor is scheduled
6) Billing

- Clinical Testing Services
  - Help identify and guide clinical care for patients by giving healthcare providers insight into the underlying genetic component of a disease or health condition
  - Can be used to confirm a diagnosis, provide better understanding of a prognosis, and direct medical management
  - Can support healthy pregnancies with carrier screening and preimplantation testing
  - Can determine someone's predisposition to cancer, cardiovascular conditions, and more
  - A clinician can subit a test request form or a patient can let their clinician know
- COVID-19 Testing
  - Only a healthcare provider can collect the specimen necessary to test for COVID-19
  - This test has not been FDA cleared or approved however it has been authorized by FDA under an EUA for use by authorized labs
  - This test is authorized only for the detection of nucleic acid from SARS-CoV-2 and not for any other viruses or pathogens
- Forensic Testing & Genealogy Services
  - Uses familial matching within the FamilyTreeDNA database to identify individuals who may be related to an unknown sample and sometimes the identity of the unknown individual associated with the sample
  - Gene by Gene and FamilyTreeDNA can provide forensic genealogy services to law enforcement for violent crimes against individuals or to identify the human remains of a deceased individual
  - Cases are submitted and the Gene by Gene team reviews case files and provides an evaluation of the suitability of the sample prior to testing
- Immigration DNA Testing
  - DNA testing service that assist with the immigration process between the US and countries around the world
  - Has experience working with embassies around the world
  - Each client with be provided with an experienced professional who offers guidance throughout the testing process

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    - Most often, sample collection methods isa buccal swab, however, if embassy requires blood, will also work with blood stain cards
    - Must contact Gene and Gene for pricing
- Paternity Testing
    - Court admissible DNA test - $425 USD
    - Personal use test - $198 USD
- Maternity Testing
    - Court admissible DNA test - $475 USD
- Research Genetics
    - Helps researchers gain in-depth knowledge to better understand the role of genetics through affordable exome and whole genome sequencing and genomic data management
    - Research partners are provided with
        - Services are HIPAA compliant and conducted in a CAP/CLIA accredited laboratory
        - Illumina NovaSeq 6000 instrument
        - PCR-free, Whole-Genome Sequencing
        - Data provided as FASTQ
        - Array services

News

- Gene by Gene announced on April 30, 2020 that they will begin performing a diagnostic test to detect nucleic acid from the SARS-CoV-2 virus that causes COVID-19 to answer the call for additional testing capabilities in the U.S.
    - The test produces results in less than 24 hours of a specimen arriving at the Gene by Gene lab
- Numerous reports describe the growth of the Direct-to-consumer Disease risk and Health DNA Test market and lists Gene by Gene as a key player
- https://sacramento.cbslocal.com/2020/08/04/genetic-genealogy-leads-to-mothers-arrest-in-her-babys-1988-killing/ - Aug 4, 2020
    - A women was arrested in the death of her newborn baby in San Francisco 32 years ago
        - The case was taken up last year with the help of Gene-by-Gene and after extensive genealogy research, surveillance, and DNA collected from the assailant led to an arrest