Whole-Genome Sequencing as an Asset for Life

Whole-genome and whole-exome sequencing–based consumer genomics companies are entering the market, offering a genomic view for life-long genetic assessment.

Introduction

Surrounded by the Apennine Mountains in the Aterno River Valley, L'Aquila, Italy isn't the first place you'd think of as the site of a direct-to-consumer (DTC) genome sequencing company. Yet, its central location within Italy made it the perfect place for Dante Labs to establish its laboratory headquarters.

According to CEO and co-founder Andrea Riposati, Italy was chosen for two reasons. "First, there is long tradition of studying genetics in Italy and we knew that it was home to a highly skilled workforce of individuals in genetics, bioinformatics, and biotechnology," Mr. Riposati said. "We also wanted the lab to be inside the European Union so that customers would know that their data were secure and protected by European privacy laws, such as the General Data Protection Regulation (GDPR). European privacy regulations are the most mature in the world."

The focus and mission of Dante Labs is to "unleash the power of whole-genome sequencing (WGS), enabling customers to gain the benefits of data from their entire genome." According to Mr. Riposati, "a person's genome is an asset for their entire life. Providing people with access to their whole-genome data can help them lead longer, healthier, and fuller lives."

iCommunity spoke with Mr. Riposati about Dante Labs and its whole-genome and whole-exome sequencing (WGS and WES) DTC testing services, the value the NovaSeq™ 6000 System provides, the potential for genomic data to change the face of rare disease research, and the future of the DTC genomics market.

Q: What was the motivation behind starting Dante Labs?
Andrea Riposati (AR): I had a friend in New York who was having difficulty obtaining a WGS test for himself. For help, I reached out to another friend, Mattia Capulli, who was active in biotechnology and genetics studies. Together, we realized that although genetic technologies had advanced and there had been significant innovation in genomics, individuals weren't able to access WGS tests easily. Together, we founded Dante Labs with the goal of offering WGS DTC testing to consumers internationally.

Q: How did your backgrounds help in founding and growing Dante Labs?
AR: Dr. Capulli is an Assistant Professor of Biotechnology at the University of L'Aquila, where he managed a genetic lab studying rare disease. He focused on establishing the lab, testing infrastructure, analysis pipeline, and, more importantly, the technical recruiting pipeline at Dante Labs.

I worked at Amazon and Muse Technologies, a data analytics platform company. My Amazon experience enabled us to turn Dante Labs into a global business quickly and to establish a successful international logistic network to make sure that we could deliver the same quality of service to people living in New York or Rome as we do for people living on remote Pacific Islands. Working at Amazon and Muse also helped me understand the value of the user. Dante Labs is a user-centric company. We have the end user in mind as we launch new products and create services.

Q: What makes Dante Labs unique in the consumer genomics testing market, compared with companies such as Ancestry or 23andMe?
AR: Unlike other companies that perform targeted array analyses, we specialize in a WGS DTC offering where we're analyzing 100% of a person's DNA. We believe that WGS is the genetic testing methodology to use because it's the most comprehensive. It's also the best technology available on the market and provides access to the latest developments in science.

WGS is more expensive than arrays, and data interpretation is more complex. By sequencing high volumes, we were able to build our own sequencing center and run the NovaSeq 6000 System at high capacity, lowering the cost of sequencing. We addressed the complexity of data interpretation by creating our own software to generate reports. Our customized reports combine health and wellness information that users provide with the genetic analysis data. The report can be useful to them. In the process, we've made WGS more accessible to everyone.

Andrea Riposati is the CEO and co-founder of Dante Labs in L'Aquila, Italy.

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Q: Why do you view WGS data as an "asset for life"?
AR: As of today, only 10% of the genome has been studied. We know little to nothing about 90% of the genome. Yet, every month, more genomes are sequenced, new studies are published, and more findings become available. In time, our customers will be able to discover more about their DNA. The earlier in someone's life that it's analyzed, the earlier they have access to useful information about their genetic makeup. This is information that can translate into actionable insights on how someone could change their lifestyle to feel better, prevent diseases, avoid adverse reactions to food or drugs, and tailor their physical activity for optimal health. As more genetic variants are identified, they can receive updates about their genome for the rest of their lives. We just introduced a subscription service where customers can receive these updates on a monthly basis.

Q: Who are Dante Labs' target customers?
AR: Our target customers are people who are focused on their health and preventive health care. They generally want themselves and their families, especially their kids, to have access to tools that will enable personalized preventive health care. Knowing their whole genome gives them the information needed to live their lives and take care of their health in a personalized way.

Q: What about your offering appeals to those customers interested in wellness and preventive health?
AR: There are two types of people in the world in terms of how they view health care. First, there are those who when they get sick, go to the doctor or pharmacy to get a drug and they feel better. This group waits until they are sick before acting on their health.

The second category includes people who are focused on preventive health care so they can intervene before they get sick. For example, we have a customer who found out he is predisposed to hemochromatosis, so he now has reduced the amount of iron in his diet to reduce his chances of getting this disease. Instead of worrying about the trending health issue that everyone else is talking about, he's focused on the condition that is most relevant to him.

People also like knowing their potential reaction to medications. Some drugs work better or worse in different people, and often the reason is genetic. By harnessing pharmacogenomic information, people and their physicians can understand the best dose for particular drugs, or which drugs they might want to avoid completely.

Q: How do you market to your customers?
AR: We use digital advertising and word of mouth to communicate the benefits of Dante Labs. Today, we are in about 90 countries, including some remote Pacific Islands. Some of our customers discover us through their friends and some of them through targeted advertising online, such as Google. We offer free shipping to everyone, so someone who is in the middle of the ocean does not pay more than someone who lives 500 meters from our laboratory.

Q: What types of tests do you offer?
AR: We offer WGS-based tests at different coverages, going from a 5× to our popular MyFullDNA product with 30× coverage. From there, people can decide to upgrade for even more analysis, such as WholeGenomeZ that includes WGS and in-depth exome analysis at 130× coverage. The variety of tests enable people with different needs to access different types of coverages. Also, people can start with a simple WGS test and receive reports on wellness initially. Then, anytime they want, they can upgrade their analysis without having to send us another sample.

Q: What are the different variants or markers that your tests assess?
AR: Today, we perform WGS and WES to identify single nucleotide polymorphisms (SNPs), large structural variants (SVs), and copy number variations (CNVs). In the future, we're looking into performing carrier screening and developing tests for predispositions for homozygous and heterozygous variants and pharmacogenomic biomarkers.

"We believe Illumina NGS systems have the best accuracy, precision, standardization, and reproducibility of results."

Q: Why did you choose Illumina and the NovaSeq 6000 System?
AR: Illumina has the same corporate values that we have. Both companies believe in the power of the whole genome to improve human health. We believe Illumina NGS systems have the best accuracy, precision, standardization, and reproducibility of results.

The NovaSeq 6000 System is a more scalable technology than anything else available, even more scalable than the previous Illumina machines. For example, most labs offer an eight-week turnaround time. A few labs offer six-week turnarounds. The NovaSeq 6000 System enables us to offer results in two weeks, and we are about to start offering a one-week turnaround time. The system has enabled us to grow quickly and offer premium turnaround time services, while analyzing both WGS and WES in a flexible and dynamic way.

Illumina Technical Support has been amazing, enabling us to start using the NovaSeq 6000 System immediately. The team helped us establish our bioinformatics pipeline and set up our new sequencing center.

Q: What software pipeline are you using to analyze your data?
AR: We have a scalable, proprietary software built on top of Amazon Web Services (AWS). We use the DRAGEN™ Bio-IT Platform to generate and analyze our VCF files and use our software to create and deliver reports to our users quickly.

We have begun introducing reports in different languages, including English, Italian, and German, with more languages to come. These reports are created automatically and dynamically by our software so that people in different countries can understand our reports in their native language.

Q: How do you make sure that the results you provide are accurate?
AR: We tested the hardware and software to International Organization of Standardization (ISO) standards to make sure that the results have a high degree of reproducibility. We make sure that we follow the best guidelines in terms of quality that we can give to our users.

Q: Can a customer specify which information that they want to receive on their reports?
AR: Yes, people can elect not to receive certain information, such as findings about conditions for which no cure exists currently. Some people are interested in WGS testing for specific conditions, such as diabetes, but they might not want to know if they have a predisposition for Alzheimer's or Parkinson's disease. We let them know that this information is always available to them if they change their minds in the future.

For those who are interested in all the findings, we provide guides to help them understand the limits of genetics and the technology. We want to make sure that our customers understand that if they have a predisposition to a certain condition it does not mean they will necessarily be diagnosed with it tomorrow. Lifestyle can play a role in the onset and progression of some diseases. We also encourage our customers to review the results with their doctor.

Q: How do you store your customer data and protect customer privacy?
AR: All our data are encrypted and stored following best practices and guidelines from the United States and Europe. In addition to what's required by law, we have introduced security measures that provide an extra layer of privacy for our users. For example, we identify reports only by a kit number, never a customer name. This way, if a customer prints a report and leaves it at a doctor's office, the report cannot be associated with them by name. If a customer wants to retrieve their data online, they log in to our website with their kit number.

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Q: Dante Labs is conducting some research with data that customers agree to share. What types of studies are you performing?
AR: We are conducting research studies in rare disease, currently neurological diseases such as epilepsy. We have found this to be an area where WGS could bring significant benefit. In these studies, people have consented to have their data used in an anonymized way. The goal is to identify unknown variants and publish them to increase our knowledge about rare genetic diseases.

In the future, we would like to work with universities to grow this part of our business. We would like to expand our research studies into other areas, such as connective tissue diseases. Ideally, universities will conduct the studies using our data and we can focus on creating new services for our end users.

Q: What are your plans to expand the presence of Dante Labs in the DTC genomics market?
AR: Our plans are to develop and offer more reports and tools for people so that they can receive more benefit from WGS testing. We're also planning to invest more in education so that people are aware of the benefits of WGS and that genomics can become a well understood research area. We'd even like to see more people studying genomics in school.

We'll continue to offer tailored services through customized offerings. We're focused on reducing the cost of sequencing further and offering faster turnaround times. We want to scale the business so that we can manage peaks in demand.

To learn more about the benefits of WGS testing, visit www.dantelabs.com

Learn more about the systems mentioned in this article:

NovaSeq 6000 System, www.illumina.com/systems/sequencing-platforms/novaseq.html

DRAGEN Bio-IT Platform, www.illumina.com/products/by-type/informatics-products/dragen-bio-it-platform.html

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