

Innovation at Illumina: The road to the \$600 human genome

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Illumina is an applied genomics technology company that was founded in 1998 with the mission statement: 'To improve human health by unlocking the power of the genome'. Over the past two decades, Illumina has developed high quality, cutting-edge, innovative technologies that are used in disease research, drug development, and for the development of molecular tests. We work across 115 countries and continue to strive to make our solutions simple, scalable and accessible to as many life sciences researchers as possible. Achieving the \$600 dollar genome has been an exciting and pivotal journey that many thought would be next to impossible to achieve, but significant drops in the cost of sequencing are now enabling unprecedented advancements in science and impacting almost every aspect of human health. Here, we present an overview of our interest and involvement in the field of genomics and our future research priorities.

ACCESSIBILITY TO GENOME SEQUENCING

Genome sequencing has fuelled the discovery of genes associated with diseases and the identification of new variants tied to phenotypes. Through comprehensive DNA exploration and studies, researchers have been able to create maps of gene variations related to health, disease, and drug response, build important databases and catalogue significant variances for future applications.

Historically, high costs

meant that DNA studies were unattainable to many researchers, particularly those working on diseases, populations and population diversities using large sample sets.

Genome sequencing gives you a high-resolution microscope. Reducing the price of technology opens up technology and technological advancements, and that opens the door for how powerful a genome can be and what that can mean for humanity.

The progress and use of genome sequencing have advanced with the help of technological innovations that have improved the speed and quality and reduced the associated costs, meaning that sequencing is feasible with an average research budget. At Illumina, we understand how important it is for life sciences researchers to include genomic research as a tool to discover new ways to inform and impact the health and life of patients around the world.

150 YEARS OF GENOME SCIENCE

The first milestone in history of genome science was in 1871 when Friedrich Miescher discovered 'nuclein' (that we now know is DNA). Since then,

key events that have helped to advance genome science include the discovery of the double helix structure of DNA in 1953 by James Watson and Francis Crick (with contributions from Rosalind Franklin and Maurice Wilkins), and the development of sequencing methods by Fredrick Sanger to sequence the first full genome. The first draft of the human genome was sequenced in 2001 and the completion of the Human Genome Project followed in 2003. The first next-generation sequencing (NGS) technology was introduced in 2007, which greatly reduced the time taken to sequence DNA. When the 1,000 Genomes Project launched the following year, in 2008, the aim was to sequence the genomes of 2,500 people. By 2010, sequencing systems offered higher throughput capabilities that could generate more data points, faster and more efficiently, reducing the cost of genome sequencing from what could sometimes be as high as six to seven figures to about US\$10,000.

The pivotal leap in genome technology that helped lead to the \$1,000 genome was in 2014, when improvements were made across the sequencing chain. Enhancements in the chemistry, imaging, optics, software and analytics helped to create high-efficiency dual system imaging sequencers that could double the output without changing the cost of preparing a flow cell.

Illumina has contributed to the development of technologies needed to usher in an important era in which sequencing can be

incorporated into a large variety of research studies and clinical-related tests with turnaround times and economies of scale. The advancements have made it possible to image on dual-surfaces and process multiple flow cells, and huge increases in densities have meant multiple levels of the genome could be processed – up to two genomes per run – along with numerous other high throughput methods such as exome and transcriptome sequencing.

Reducing costs expands the reach for those who can do really great discoveries with it. By driving more discovery, you're shifting and broadening who you're impacting. With new technologies, we're realizing the opportunity to sequence even deeper, and customers and patients benefit most.

Illumina's NGS has helped to revolutionize genomics research and has wide applications in fields such as infectious disease, oncology, genetic disease and agriculture and in settings such as clinics, hospitals, research laboratories and government agencies.

PROGRESSION FROM THE \$10,000 GENOME TO THE \$600 GENOME

This year, genome sequencing celebrates its twentieth anniversary and an evolution that has helped lead to remarkable and rapidly accelerating progress and turning points in healthcare. Today, a human genome can be sequenced for \$600, with some predicting that the \$100 genome is not far behind. The declining cost of human genome sequencing has made it possible for the research and clinical world to apply their expertise in the study of diseases and phenotypes.

The technology available today is life saving and users of it have the opportunity to make a real impact. Now we are seeing genome sequencing put into practice because it's no longer a \$10,000 genome.

Healthcare providers are in a position to offer whole-genome sequencing to large patient populations at an affordable cost. Laboratories of any size are implementing ways to simplify and stabilize workflows to genome sequence more frequently.

Illumina's research focuses on developing the technological tools that will enable researchers to continue to make scientific advances in genetic disease, common genetic disorders, population genetics, and basic cell and molecular biology relevant to clinical applications such as reproductive health, oncology testing, infectious disease testing and surveillance.

THE FUTURE FOR WHOLE-GENOME SEQUENCING

Product development at Illumina

has included whole-genome sequencing, a tool that can be used in diagnostics to identify the causative variant of a disease, among other applications. The value of whole-genome sequencing is gradually reaching a price point realistic for widespread adoption and studies.

Exome sequencing is more affordable and has found its place in genetic disease studies. Transcriptome sequencing and single-cell resolution have become less expensive and significantly more useful when the research calls for looking at the individual expression of each cell, rather than all cells together.

Illumina's commitment to the research and development of analytical tools extends to the field of epigenetics. Epigenetics, historically expensive, is emerging in the field of oncology as a critical and potentially game-changing research method in the study of methylation and its presence in a patient's genome for possible predisposition to cancers.

The genome is the operating system, and the transcriptome gives it the color. From there you can get down to cell specific true expression and marry it with genome sequencing to answer biological questions. The more channels the input has, the better the research will be.

THE IMPORTANCE OF INNOVATION TO DRIVE GENOMICS-POWERED PRECISION HEALTH

Illumina's vision for the future is to improve human health. Part of that vision is to provide

access to genomics, which is why the company is developing programmes and partnerships to give access to genomic technology to benefit as many people as possible through improved diagnostics and therapeutics.

Cancer is a disease in the genome, but where do you start when it is peppered with mutations and noise? The key is understanding that level of detail in the cancer genome, which will ultimately lead to understanding what variance a person may be dealing with, and then from there you look at populations with similarities of patterns and link it to therapies and detection.

The big promise of genome sequencing is to facilitate the analysis of millions of samples. To detect structural variants and to determine the impact of variants in the non-coding genome has its challenges because whole-genome sequencing requires substantial preparation. However, the more comprehensive the database becomes across a disease state, the better understanding there is of a disease and the more effective and precise the therapies will be for patients.

The big promise of sequencing technology is high accuracy power and operating efficiencies at the best price possible to fuel in-depth research across the scientific spectrum and support the analysis of genetic variation and function.

Illumina's goal is to continue to deliver innovative and exceptional sequencing technologies that will further the work of all scientists engaged in groundbreaking research. Every breakthrough in genomic science creates new possibilities to expand and push the boundaries across the life science spectrum. The key is to continue to unlock the power of the genome for human health today and future generations to come.

The trajectory enables us a future where we should no longer be constrained at just looking under the tiniest spotlight. We have the opportunity to look at the whole-genome, the single cell, and we can go as deep into biology as the question begs it to go to make those discoveries that will inform the next therapeutics, end diagnostic odysseys, resolve cancers and more. The technology can't just be generating data anymore, it needs to be generating insights.

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