Interview: Johnsee Lee PhD – Founder, President & CEO, Personal Genomics / Quark Biosciences, Taiwan



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Johnsee Lee, founder, CEO, and president of Personal Genomics and its sister company Quark Biosciences, provides insights into the company's proprietary Optoelectronic Sequencing (OES) technology, which can perform whole genome sequencing thousand times faster than existing technologies and increase read length twentyfold in comparison to sequencing products currently on the market, while he expects a prototype to be ready before the end of 2017.

What motivated you to found Personal Genomics in 2011?

Most genomics companies based in Taiwan use sequencing products and technologies developed by multinational companies and could be – in this regard – considered more as service providers than technology developers.

Personal Genomics' vision – on the other hand- is truly to bring to the world groundbreaking sequencing technology and devices. The company's history actually started at Taiwan's Industrial Technology Research Institute [ITRI], where I served as President from 2003 to 2010. In 2008, we notably set up the "1000 G" project with the ambition to develop a sequencing technology that would bring human genome sequencing cost down to the USD 1000 mark.

The launch of this ambitious project only came five years after the completion of the Human Genome Project (HGP), the USD 3 billion, publicly funded, international scientific research project that became the first to fully sequence human DNA thanks to the collaboration of more than 40

research centers and universities in various countries. In the mid-2000s, the technology's pace to sequence a complete human genome was still extremely slow, devices were extremely cumbersome while the cost of a single sequencing was still around USD 5 million – highlighting how ambitious ITRI's "1000 G project" was at that time.

After having spun off ITRI's proprietary technology in 2011 and set up Personal Genomics to further advance its development, we remain as ambitious as before, as we now hold the overarching objective to bring sequencing cost below the USD 100 mark while tremendously reducing sequencing time. In the meantime, we want to develop devices that could be easily handled by physicians in hospital and clinical settings – and not only by PhD researchers specialized in genome sequencing.

In the grand scheme of things, my vision is to make genome sequencing and its applications more widely available and affordable to patients around the world. In a way, we want to replicate Taiwan's achievements in the IC industry, where our domestic industry significantly contributed to make computers and smartphones largely available to a great share of the world's population.

What sets apart your technology and make you believe it could become a new industry standard?

Genomic analysis is usually divided into two main categories. First, comprehensive profiling such as whole genome sequencing, which allows the determining of the complete DNA sequence of a living organism's genome; and, second, biomarkers detection such as FISH or PCR (polymerase chain reaction) technologies, which stands a less comprehensive, but more focused approach – on which Quark Biosciences [the sister company of Personal Genomics, e.d.] is focused.

Personal Genomics and Quark Biosciences prototypes are all based on our proprietary Optoelectronic Sequencing (OES) technology. We believe this technology will replace the currently used NGS (Next Generation Sequencing) technology, which came as the evolution of the original Sanger sequencing approach used for the Human Genome Project (HGP).

OES technology is based on an on-chip in-situ optoelectronic detection for direct base calling and a novel sequencing chemistry that ensures high accuracy and long reads. In the meantime, OES's localized detection by light coupling also enhances overall yield. Overall, our proprietary square-inch chip is capable of real-time detection of millions of single-molecule sequencing reactions in seconds, which explains why we are confident to soon bring onto the global market a breakthrough, simple, compact, and cost effective sequencing technology.

Concretely, we expect our OES-based devices to display major advantages in comparison to existing NGS technology. For example our target is to reduce sequencing speed from 300 to 0.3 seconds/base, meaning we will be able to complete a whole genome sequencing within an hour while existing products need around three days. Furthermore, OES enables read length above 3000

bases, while current NGS products are limited to around 150 bases. Although it is hard to compare sequencing prices between two technologies that display such different capacities, we also want to ensure overall sequencing cost with our OES technology would be less than a third of these displayed by existing technologies and devices.

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We have already applied to more than 150 patents globally and around 90 have already been granted to the company. Our IP portfolio covers the three main areas of our technology, including its chip and system (the OES system concept and its applications, its near-field optoelectronic detection system, as well as the excitation light source and waveguide design), our in-house developed chemistry and protocol (single molecule sequencing chemistry with confirmation step, novel nucleotides and polymerase, our unique library construction, efficient sample loading & processing, as well as the localization of detection by waveguide light coupling). Finally, we also applied for patents covering our algorithm, including gene identification with a multi-junction-photodiode and the consensus sequence from redundant reading.

After more than five years of intense R&D efforts, we now expect our first prototype to be ready before the end of 2017, while we will start working on the design of different devices that will perfectly tailored to all market niches, applications, and end-users we identify.

What kind of applications do you envision for your OES-based devices, considering they will make genome sequencing tremendously faster, cheaper, and easier to be conducted in hospital and clinical settings?

Thanks to DNA sequencing, we can develop personalized medicine based on gene mutations of the cancer cell. This approach is already relatively mature for lung, breast, and liver cancer. For example, more than 30 different types of lung cancer have already been identified, meaning that clinicians are able to adapt treatment solutions to the DNA mutation identified.

Furthermore, genomic sequencing also allows differentiating tumor from healthy cells, making it a powerful diagnostic tool if widely available and affordable. Physicians could also conduct more precise treatment monitoring, control treatment efficacy, and detect early signs of remission or drug resistance. Naturally, technology improvement would also enhance early detection capacity (thanks to liquid biopsy, a non-invasive, very convenient technology that is not particularly mature yet) and prevention, based on the detection of inherited faulty genes.

Overall, as sequencing becomes faster and cheaper, the possibility that every individual could have his own genome sequenced is turning into a reality, and the personalized and preventive healthcare era is about to unfold. We then expect sequencing technologies to expand from the research setting to an increasing number of clinical applications, including personalized medicines, virus control and also prenatal screening – an area that is already relatively mature – but also food

safety. In this vein, our technology platform could be used on a broad scope of applications that goes beyond human applications, as all living organisms hold nucleic acid sequence within DNA or RNA molecules, meaning that sequencing technology could also be applied to bacteria, viruses, and plants for example.

In this regard, findings of studies conducted by BCC Research Market Forecasting 2013 and MarketsandMarkets Report 2013 forecasted that the global sequencing market would increase 38.6 percent CAGR between 2013 and 2017 to reach over USD 6.5 billion, while overall revenues generated by applications in the clinical field would soon overcome the research, academic, and government fields.

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Moving forward, what kind of partnership strategy are you considering implementing?

We are already talking with leading healthcare and biopharmaceutical companies, which are looking for the most pioneering sequencing technologies. Their interest encompasses both the design of personalized medicines as well as the joint development of companion diagnostics. Drug development is rapidly evolving, and genomics sequencing is largely nurturing this ongoing disruption: a better understanding of genomics would allow these companies to develop more effective drugs and better design clinical trials, prompting these companies to team up with innovative sequencing companies throughout their drug development process or develop more comprehensive partnerships to eventually access specifically-developed sequencing platforms, which will be perfectly tailored to their own needs and products.

The number of companies developing innovating sequencing technologies is extremely limited, while most sequencing technologies used today were developed by a few US-based technologies, such as Illumina. As a matter of fact, Personal Genomics is one of very few companies in the world currently working on brand new sequencing technologies.

Although our technology has already drawn the interest of some of these biopharmaceutical giants, we remain focused on our own milestones, as we are well aware that the critical next step in these potential collaborations will be to prove we have successfully developed a convincing prototype. Nevertheless, our development model is always based on partnerships.

Developing ground breaking sequencing technologies truly stands as our company’s core competence and the area in which we want to concentrate our efforts and resources. In this regard, we will then partner with specialized companies for other parts of the sequencing process, such as a sample preparation or data interpretation. If we want to sell our products in clinical settings, we will also need to conduct clinical trials in different markets, which – for our kind of devices – will fortunately be much faster than for drugs. Nevertheless, bringing our product into hospitals and clinics also requires to developing a very specific marketing and sales network, which all innovative

pharmaceutical companies already hold – strengthening the win-win relationship we could then build by partnering with these pharma partners.

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