

### QIAGEN - SAMPLE TO INSIGHT

### The molecular revolution

A scientific revolution is rapidly evolving our understanding of DNA and RNA – the building blocks of life. It's affecting us in ways many people don't even realize.

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### The challenge

Gaining access to valuable molecular insights – and understanding their impact – remains elusive and challenging.







Costly

Lengthy

Unreliable

THAT'S WHY QIAGEN EXISTS

Every day we help more than

500,000

customers gain the valuable molecular insights they need



HOW WE DO IT













Offer a targeted product portfolio to enable insights from samples for virtually any application involving the building blocks of life. Keep a finger on the pulse of innovation to turn the latest scientific breakthroughs into useful products. Bring together 5,000 passionate QIAGENers who are driven by the impact of their work and to excel in helping customers exceed their own expectations.

Extend our global reach so we're everywhere our customers are – in countries around the world and even in space.



OUR VISION:
MAKING IMPROVEMENTS IN LIFE POSSIBLE

We live in an age of scientific discoveries and rapid progress into the building blocks of life – DNA, RNA and proteins.

These advances are improving our everyday lives, changing the way how people are treated for diseases like cancer, tuberculosis and other conditions, helping to find new medicines and even safeguarding the public.

But unlocking new answers from the incredibly complex world of biology – and turning them into breakthroughs that impact our lives – remains elusive and challenging.

QIAGEN exists to support this quest, helping more than 500,000 customers around the world to gain the valuable molecular insights they need to improve healthcare and advance science. Our differentiated Sample to Insight solutions are used along the continuum from basic research to clinical healthcare and industrial applications to unlock insights easier, faster and more reliably than ever before.

Our passionate employees – known as QIAGENers – care deeply about the impact of their work. They are trusted advisors and experts committed to understanding the needs of our customers and tailoring our Sample to Insight portfolio to help them exceed their own expectations. We are embracing the spirit of digital transformation, working to improve our speed and agility in supporting our customers while creating even more value.

QIAGEN is tackling the bigger questions of our age and helping solve biological challenges that affect us all. This is an enormous challenge – but one that energizes us to excel.

It's how we help our customers to advance from Sample to Insight and ultimately achieve our vision of making improvements in life possible.

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PASSION
ENGAGEMENT
QUALITY
INNOVATION
INTEGRITY

The QIAGEN identity and what it means for our employees





# "Our solutions, woven into the daily work of healthcare and science, play a growing role in many areas of life."

— Conversation with Peer M. Schatz on the rapid expansion of genomic applications, QIAGEN's achievements in 2017, and the forward-looking strategy to create value with differentiated Sample to Insight solutions that are helping customers to exceed their own expectations in finding valuable molecular insights.



PEER M. SCHATZ, CEO QIAGEN N.V.

### How do you see the business environment evolving for molecular testing?

Hardly a day goes by without news of some dramatic discovery or new application of genomics, that is, understanding the molecular building blocks of life - DNA, RNA and proteins. QIAGEN is a key driver of this revolution. Because of the expertise of QIAGEN teams around the world, we have built deep relationships across the continuum from science to its application in routine healthcare: basic researchers, pharmaceutical and biotech and other companies of all sorts, and to a significant degree already also physicians who are becoming more savvy about how genomic insights can impact the way they care for their patient. Our solutions, woven into the daily work of healthcare and science, play a growing role in many areas of life. Much has been accomplished, but some of the world's most pressing challenges lie ahead. We are very excited about the future of molecular testing and the role we intend to play.

### What is the Sample to Insight strategy that you are pursuing?

Sample to Insight means that any discussion, be it in front of a customer on in our product ideation phases, starts with insights our customers are seeking, how they define a valuable insight and what holds them back from achieving their goals. Unlocking new molecular insights is elusive and challenging. At the same time, the results can be a matter of life and death. QIAGEN's goal is to help scientists and healthcare professionals to generate the insights they need in a faster, better and more efficient way – by putting the value of their insights and the applications to get there at the center of our decision making. Success is defined by how well we understand their applications and design them so that our customers are successful, and not by how well customers understand the features of our products. We take customers from a raw sample such as blood or tissue, through analysis with the best assays and the right instruments to find their answers – useful, actionable insights. Our approach is beginning with what will define value and then creating a complete solution to get there.

## "WE ARE DEDICATED TO TRANSFORMING QIAGEN'S BUSINESS TO CREATE VALUE."

### As we move into 2018, what are your perspectives on this past year – and the future?

We are dedicated to transforming QIAGEN's business to create value, and 2017 was a great year. We delivered on our growth ambitions – a portfolio of differentiated Sample to Insight solutions that serve rapidly growing market needs – and met our goals for accelerating sales and earnings. We continued to drive our digital transformation and build our global team, with the deepest and broadest expertise in the industry. Our worldwide presence is thriving, both in well-established and emerging markets. We executed our efficiency initiatives and improved profitability. Most important, QIAGEN innovation keeps delivering new solutions for our customers' needs. We are well on track to achieve our mid-term goals for outsized growth as we approach 2020.

### Turning to specifics, how does tuberculosis testing fit into QIAGEN's growth plans?

Tuberculosis persists as the world's single most deadly infectious disease, with more than 1.6 million people dying each year. Our QuantiFERON-TB tests deliver highly accurate detection of TB infection in its latent stage, helping to effectively address this global health problem. In 2017, we successfully launched the fourth-generation test, QuantiFERON-TB Gold Plus, in the United States and Japan after introducing it across all other major markets. And there is still ample room for growth. We have reached only about 15-20 percent of the total addressable market of about 65 million tests a year. In 2018, we are taking further steps to grow our QuantiFERON franchise, such as partnering with DiaSorin to offer a highly efficient automation option for customers to process QuantiFERON-TB tests on the popular LIAISON platform, which has access to a broad menu also beyond QuantiFERON. QuantiFERON-TB continues to grow at a rapid pace, and we are on track to achieve \$300 million in sales in 2020.

### What is your strategy for growing QIAGEN's position in next-generation sequencing?

We are expanding our NGS franchise with a broad portfolio of universal products that run on any sequencer, and our GeneReader NGS System is building good momentum as the world's first complete Sample to Insight solution for nextgeneration sequencing. Our universal NGS products include differentiated technologies for challenging samples such as liquid biopsies and microbiomes, plus highly reliable QIAseq "Digital NGS" gene panels for clinical research. Some panels are pre-designed for widespread use, while others are customized for specific purposes. Customers continue to respond very positively to our GeneReader platform, which is reflected in a growing number of placements in more than 30 countries worldwide. In 2017, we accelerated Gene-Reader's commercialization in China by creating a joint venture with Maccura, a leading in vitro diagnostics company in that market. Overall, our NGS sales surpassed \$115 million in 2017, and we expect to exceed \$140 million in 2018.

### How would you describe QIAGEN's role in the growth of precision medicine?

We are the market leader in developing companion and complementary molecular diagnostics that enable more precise clinical decision making. In 2017, QIAGEN added a record number of co-development partnerships in Personalized Healthcare, passing a milestone of 25 master collaboration agreements with pharma and biotech companies. We are also pioneering the development of NGS-based companion diagnostics to guide the use of immuno-oncology drugs in cancer, launching two partnerships in 2017 with pharma leaders in this rapidly growing field. Precision medicine is routine today in cancer, but also expanding to a range of other diseases that can be targeted with genetically targeted therapies. We expect to achieve more than five FDA submissions and/or U.S. launches in 2018.

### Your flagship automation system QIAsymphony is going strong in terms of placements and utilization, but do you think its growth trend is maturing?

Quite the contrary, and we see a long runway for QIAsymphony to continue its growth. We had a very strong year in 2017, substantially beating our goal of more than 2,000 cumulative placements and achieving double-digit growth in consumables. In the 10 years since we launched the first QIAsymphony module, this revolutionary system has become the leading automation solution for molecular sample technologies and complete Sample to Insight workflows. We think the future is bright for PCR (polymerase chain reaction) and expect QIAsymphony to grow alongside our other platforms. Customers have a wide variety of needs in molecular testing, and there is no one-size-fits-all solution. Our 2018 target is to exceed 2,300 placements, with further growth in content menu and consumables.

### You recently announced the acquisition of STAT-Dx and plans for a new platform that can perform multiple genomic tests simultaneously. Can you explain?

We are excited about our agreement with STAT-Dx, a privately held company that has developed a next-generation solution for syndromic testing, an attractive, fast-growing market for unraveling difficult to diagnose sets of symptoms. We intend to introduce a fully integrated solution called QIAstat-Dx for molecular analysis of syndromes and expect to launch the first two assays, extensive multiplex panels for respiratory infections and gastrointestinal syndromes, in mid-2018 in Europe and 2019 in the United States. Already using proven QIAGEN technologies, QIAstat-Dx is highly synergistic with our portfolio and channel capabilities, adding a promising new pipeline to accelerate our growth.

### How do traditional sample technologies play a role in QIAGEN's growth strategy?

They play an absolutely critical role. We are the world's leader in differentiated technologies for sample technologies. Wherever you look in molecular testing – diagnostics, NGS labs, Nobel Prize-winning institutes and even forensics – QIAGEN front-end solutions play critical roles. Some 50,000 samples a day are processed with our solutions, and we continue to pursue new opportunities and innovations. We are No. 1, for example, in sample technologies for liquid biopsy applications. In microbiome research, QIAGEN has about a 75 percent market share. We also lead the industry in sample solutions for epigenetics, such as long-read RNA and microRNA. As customers identify needs that arise, we establish strong positions and integrate bioinformatics to enable Sample to Insight solutions. Differentiation and superior quality keep this business growing rapidly.

### You continue to invest in bioinformatics. How is this portfolio doing?

Bioinformatics is another fast grower. This has been a real key in QIAGEN's transformation to delivering Sample to Insight solutions. Since our Ingenuity and CLC bio acquisitions in 2013, we have integrated the industry's leading software and knowledge bases with our sample and assay technologies. We continue to acquire and integrate new software and databases such as Omicsoft in 2017. For nextgeneration sequencing, which generates massive amounts of data, QIAGEN's informatics for interpretation are a key competitive advantage. The value of genomic knowledge keeps growing as these systems aggregate and expertly curate thousands of studies and data from large patient populations. So we don't just sell hardware or "tools." Our solutions are uniquely enveloped in digital solutions which take cus-

## "WE ARE VERY EXCITED ABOUT THE FUTURE OF MOLECULAR TESTING AND THE ROLE WE INTEND TO PLAY."

tomers right through to the most valuable insights made possible by molecular testing.

### What progress has been made on QIAGEN's initiatives to increase efficiency and effectiveness? How do you keep the focus on growth at the same time as efficiency?

Focusing on growth does not mean you have to sacrifice efficiency and effectiveness. When we launched our ambitious plan to accelerate sales and earnings through 2020, we knew we had to focus on controlling costs and streamlining organizationally in order to invest more in the most promising growth areas. So we took aggressive actions. For example, we moved more back-office activities from decentralized, duplicative locations to a shared service center in Poland, where processes are more cost-efficient. In 2017, we decided to open a second shared service center in the Philippines and began migrating administrative functions there. We launched a company-wide digitization effort to better serve customers, and in 2017 we were up to about 40 percent of sales coming through digital channels. Thanks to the ongoing support of our employees, these efficiency efforts have begun to pay off, leading to improved financial results, more agile business processes and higher customer satisfaction.

### Where is the business of genomics heading in the future, five or ten years from now?

Clearly, the future will bring more and more molecular testing. It is a high-growth field driven by exponentially growing knowledge. Cancer care already is deeply influenced by genomic data. We look for molecular testing to increasingly guide medical approaches to infectious diseases, diabetes, and cardiovascular and neurological conditions. Some scientists foresee a day when everyone's genome will be sequenced at birth, providing predictive insights for better lifelong health. Applications in science and public safety are multiplying.

Molecular testing does not seem to be evolving to "one thing." It won't become, for example, just whole genome sequencing. Instead, the industry is expanding into hundreds of purpose-built applications: assays targeting single mutations, multiplex gene panels, epigenetics, PCR, NGS, whole exomes and genomes, single-cell analysis, and many other customer needs. We are still in early days, and some of the world's most pressing challenges lie ahead. As we look to the future, QIAGEN will be here, meeting customer needs and making improvements in life possible.





— Here are some fascinating breakthroughs – just some of many made in 2017. Some may hold the potential to write science history. And by the way, QIAGEN is an enthusiastic partner of researchers all over the world. Our products are used to start 50,000 experiments every day in labs around the world.

### The electric touch to heal

In the future, a single touch might be enough to save failing organs. Researchers at Ohio State University say they have found a way to turn skin cells into other tissue with just the touch of a device. The method, called tissue nanotransfection, delivers DNA or specific proteins to cells using an electric current to create channels in the tissue. The DNA then reprograms the cells. While reprogramming cells is not a novel technology - transforming skin cells into pluripotent embryonic stem cells won a Nobel Prize several years ago – this method may allow researchers to skip the conversion into stem cells. The researchers succeeded in turning skins cells into blood vessels, allowing renewed blood flow to the wounded legs of mice. While it is still too early to tell if this method will function in humans, it seems to hold enormous promise.





### **Unlocking complex secrets**

Just when we thought we had the genome figured out, it seems as if we might have been missing some of the most important pieces. Scientists are beginning to understand not only the linear placement of genes on DNA strands, but also their spatial organization that controls gene expression. Studying the genome's three-dimensional structure – for example, how DNA loops may move genes closer to enhancers – might yield new insights and therapies.

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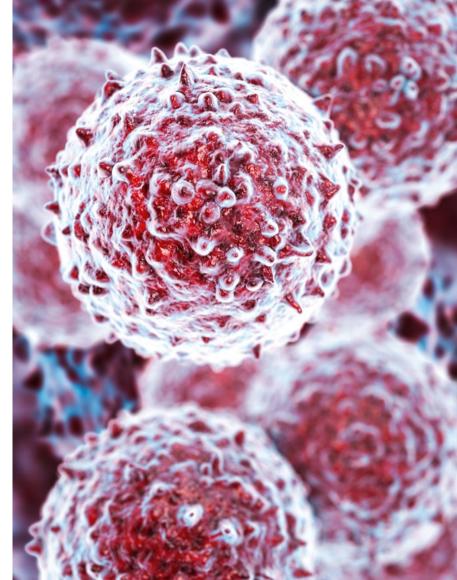
The gene editing technology CRISPR/Cas9 – dubbed molecular scissors – has caused a major upheaval in biomedical research. Now a new pair of scissors, related to the first, has been found, offering the ability to rewrite individual bases in both DNA and RNA. Why was that a major step in science? To date, more than 60,000 genetic aberrations have been linked to human diseases, and nearly 35,000 of them are caused by the tiniest of errors: a change in just one DNA base at a specific point in the genome. The hope is that the new technology, called base editing, could correct these single base mutations.

A new pair of molecular scissors

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S





### What if?

What if we could coax stem cells into making tiny replicas of organs? Wouldn't we have wonderful models to study infectious diseases as well as single gene disorders such as cystic fibrosis and those stemming from an interplay of many genes, like cancer? It turns out we can. Scientists found a way to grow these models in what *Nature* named "Method of the Year" in 2017. Organoids replicating the brain, the liver, the kidney and the retina exist, to name just a few. The breadth and width of their applications are endless. What if... organoids hold the key to curing and treating some of the most insidious diseases?





### Using the body's own firepower

The idea that a drug could use the body's defense system to fight cancer is truly revolutionary. Very different from radiation, chemotherapy and surgery, these new drugs target the body's immune system, not the cancer itself. Enabling the immune system to see and attack cancerous cells, and continuing to do so, offers a long-term response to cancer. The U.S. Food and Drug Administration (FDA) in 2017 expanded the approval of an immunotherapy drug to include tumors with a specific change, regardless of cancer type. This is the first time the FDA approved a drug based not on the body part in which the cancer occurred but on the genetic changes at the root of the tumor. QIAGEN is committed to developing diagnostic tools to identify patients who could benefit from immuno-oncology.





"I've been wanting to understand life since I was a student. Here at QIAGEN we can look at life at the cellular and molecular level; we can use our technologies to understand even the most complex processes in living organisms.

I want to be able to drive change in my work, to turn new scientific insights into real-life applications. That's one reason why I switched from academic research to a career in industry. Hundreds of thousands of scientists around the world work with QIAGEN products; that means our knowledge is multiplied – that really motivates me.

For me, passion means identifying with something that is important, that has meaning. In an organization, passion thrives on trust and openness. That creates the excitement I share with my colleagues. Instead of focusing just on their own work, everybody lends a hand and helps out coworkers. That is the QIAGEN spirit – to be part of something big."



### > 9 5 0

QIAGEN R&D employees in several Centers of Excellence are passionate about pushing the limits of possibility to develop novel Sample to Insight solutions that advance life science research and healthcare.



— Next-generation sequencing (NGS) has enabled unprecedented advances in oncology: personalized therapies are becoming possible, pathologists have gained unparalleled insights into the nature of tumors, and artificial intelligence can arrive at reliable diagnosis based on the immense data created by sequencing. Prof. Paul Hofman, a pathologist at the University of Côte d'Azur, France, wonders if doctors like him will even be needed in the future. We visited him at Nice Hospital.





A drop of DNA is pipetted onto a sequencing flow cell. Supporting continuous loading of multiple flow cells, the GeneReader workflow can be easily scaled to support larger testing volumes.

rof. Paul Hofman began his professional career as an oncologist. "I experienced it as a frustrating discipline: we always did the same thing, chemotherapy. And all the time we knew beforehand that it wouldn't work for most of our patients." It was just that nobody could say for whom it wouldn't work.

At the age of 30, Prof. Hofman switched definitively to pathology. He assumed that he would have a more varied job and at the same time provide greater value to his patients.

If he could not fight cancer, he at least would strive to better understand it. He wanted to ensure that patients received the appropriate therapy. "Today, however," Paul Hofman says with a smile, "I could imagine switching back to oncology. Since next-generation sequencing revolutionized the fight against cancer, there are so many new approaches and possibilities; for example, immune therapy. It's a really exciting time for medicine."

Today, his switch to pathology is more than several decades old. Prof. Hofman is currently in charge of the Surgical Pathology and Tumor Molecular Biology Department and of the Biobank Unit at the University Hospital of Nice.

The clinic is an architectural patchwork blanket that grows uphill and, due to the lack of space, has spread over the years into every imaginable gap on the site. At the top is a tower whose white facade is slowly graying. "Laboratoire" is spelled out vertically in large letters, one letter for each floor. Inside, its construction is as intricate as it is outside. Narrow and winding corridors, tight offices. A place in which it is easy to get lost.

Prof. Hofman looks like an image of the building, lean and tall, his lab coat no longer brilliantly white, his eyes tired – but in the corners of his mouth he has a friendly, gentle smile.

He is considered one of the leading lung cancer pathologists in Europe: a disease in which positive treatment outcomes depend on very early diagnosis. Prof. Hofman is studying, for instance, if liquid biopsy could become an alternative screening approach, allowing the disease to be detected months or even years earlier than with traditional imaging tools. In addition to his research work and managing the institute, Prof. Hofman holds functions in more than a dozen professional societies. A 70-hour week is the rule, not the exception.

### GeneReader NGS System

The GeneReader NGS System is the world's first complete Sample to Insight solution for next-generation sequencing (NGS). It enables high sensitivity detection in liquid biopsy specimens and high throughput sample processing through compatibility with the QIAsymphony automation platform. The new GeneRead QIAact gene panels are compatible with FFPE and liquid biopsies. Integrated bioinformatics provide optimized, cloud-based analysis and interpretation of NGS data. In 2017, QIAGEN released new studies at the Association for Molecular Pathology (AMP) annual conference highlighting the outstanding analytical performance and easeof-use of the GeneReader NGS System.

### **Immunotherapy**

In 2017, QIAGEN made great strides towards supporting greater use of molecular diagnostics for immuno-oncology therapies. The company has licensed novel biomarkers for microsatellite instability (MSI) and mismatch repair (MMR), and entered into a collaboration agreement with Bristol-Myers Squibb to develop gene expression profiles to help guide treatment with novel immuneoncology molecules currently under development. QIAGEN is also working on the application of its QuantiFERON Monitor (QFM) to monitor immune function. As part of the diagnosis of patients eligible for or treated by I-O therapy, QFM has the promise to provide important clues about the state of a patient's immune system.

### Immunotherapy response

TMB is the hypothesis that an increased mutation rate leads to an increased number of mutated proteins, or neo-antigens, on the surface of tumor cells, capable of eliciting an immune response. This pre-existing immune potential is a major factor that will determine whether patients derive benefit from immune-oncology treatments.

The telephone rings incessantly during the conversation; often students from all over the world want to work with him. Employees stick their heads through the door to ask a question. The tone is conversational and friendly. When asked how he endures this day after day, Prof. Hofman shrugs and grins, "With the help of 15 espressos a day, at least."

In reference to the new fascinating possibilities in oncology, of course, there is also a touch of coquetry. Next-generation sequencing is a game changer in his specialty too. The revolution in the war against cancer starts in pathology and understanding how liquid biopsy samples can be best used for screening.

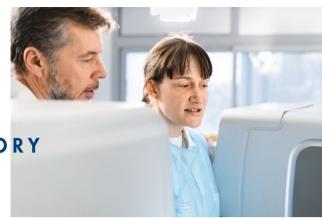
From Prof. Hofman's point of view, this upheaval starts on the third floor of his institute. While traditional laboratory medicine is practiced on the ground floor where tissue samples from cancer patients are prepared, dissected into wafer-thin slices and dyed, up here are various sequencing machines that analyze the samples genetically. Recently, a QIAGEN GeneReader NGS System was installed to help Prof. Hofman obtain the insights he seeks in his quest to advance research into better prevention and treatment of cancer.

If oncologists want to deploy precision medicine, i.e., treat patients individually based on their genomes and that of their tumors, Prof. Hofman and his colleagues will have to deliver precision pathology.

Because every tumor has genetic and immunological differences that affect how immunotherapy works, tumor sequencing makes sense in pathology. It can provide valuable data on the genetic profile of a specific form of cancer. Together with the interpretation of a patient's exome and genome, it can result in the discovery of new biomarkers.

One such biomarker, which has been associated with immunotherapy response in multiple disease types, is tumor mutational burden (TMB). TMB measures the number of mutations within a tumor genome, and tumors that harbor more mutations have been shown to have a greater likelihood of an <a href="mailto:immunotherapy response">immunotherapy response</a>. Now, Prof. Hofman is working toward developing methodologies to assess TMB in lung cancer.

### "WITHOUT NGS, A MODERN LABORATORY IS UNIMAGINABLE TODAY."



Prof. Paul Hofman

### Do all these new approaches mean that the era of glass slides and microscopes in pathology is over, Prof. Hofman?

PROF. PAUL HOFMAN No, the key is integration. There is not just one single tool in the future of cancer therapy. We need everything. Liquid biopsy, histology, bio-pathology, sequencing, clinical data, behavior, microbiome, etc., and yes, old-fashioned tissue samples under the microscope.

### What challenges do you face in your everyday work?

On the one hand, the multitude of methods gives us completely new possibilities, but they are also limited by one factor: the amount of sample material. Sometimes we have only a few hundred tumor cells for evaluation, so we cannot do one test after the other, because there simply is not enough material. Molecular biological technologies such as NGS are the only proven means to obtain answers from such small amounts of starting material.

### What about communication with the attending physicians – are you in direct contact with them?

You speak to another gap. The link between pathology and diagnosis must be made narrower. Pathology is the hotspot for everything, and I do not say that because I am a pathologist myself. But we need, for example, the clinical data to help guide our choice of analytical method, because the suitability of a method of analysis also depends on whether the patient is a young nonsmoker or a retiree of 70 who has smoked for many years.

### Why did you choose the GeneReader?

Without NGS, a modern laboratory is unimaginable today. There were calls for a better traceability of the workflow, which the GeneReader provides. We also save a lot of time with the device: processes that used to take 45 minutes are now completed in five to ten minutes. The good reports generated by the system which provide actionable insights are another reason. The operation is simple; the results are very robust. I like the restrictive panel as this ensures the most relevant results from the low DNA concentration in the samples. It really is a very powerful NGS system.

### What is the future of these systems?

In the future the interaction with liquid biopsy will be interesting. We will be able to discover a lot by NGS in blood samples. It will become even more interesting if we use NGS with combinations of blood and tissue. That is another advantage of the GeneReader – we can analyze both with the same workflows.

### What question are you currently most concerned with in your research?

It is about the constitutional genetics – the question of why some people smoke their whole lives but do not develop cancer while others do, although they never touched a cigarette.



http://bit.ly/CHUNice http://www.GeneReaderNGS.com



Laboratory technician Lalvee Salome has worked with the GeneReader since the very first day the system arrived in the lab. She values the integrated approach, which makes it easy to harness the power of NGS technology in any lab.

NGS and new therapies such as immuno-oncology are weapons that bring victory in the fight against cancer closer to reality than ever. The use of NGS is also changing the nature of medicine. More and more, doctors must mediate between technologies. Today they need to be as familiar with algorithms as they are with anatomy.

In addition, sequencing technologies generate enormous amounts of <u>data</u>, the evaluation of which has long since overwhelmed a single person. Doctors face the fact that artificial intelligence sometimes makes a more precise diagnosis out of the terabytes of data than humans could ever do.

Should the integration of all patient-related data one day become reality, could software take care of all analysis in the hospital? That would mean integrating "big data" in clinical care. Prof. Hofman says: "If we want to combine all types of diagnostics, we need to look at big data and deep, or machine, learning." After a short pause, he laconically adds, "That leads to the question: Do we want to have a doctor or are we better off just using a machine with a giant database?"

### Date

Scientists at the Simons Center for Quantitative Biology at Cold Spring Harbor Laboratory (CSHL), New York, U.S., estimated that up to two billion genetic sequences could be available by 2025. That means the technology of gene analysis will generate reams of data, surpassing all other data-producing giants - including accelerator physics, astronomy, and the current recordholder, YouTube. While YouTube and astronomy produce as many as one to two exabytes a year, the amount of stored genetic information may be as high as 40 exabytes. One exabyte is one million terabytes, about the size of one million hard drives.



## Z W ٤ ш E N G A

"Being engaged in my community is very important to me both socially and as an advocate for causes I am passionate about. I support multiple local and national causes, particularly around equal rights and human health.

At QIAGEN, engagement is a two-fold approach. So it's engagement internally but also externally with our customers. We believe that the two belong and work together. In our team, we're a kind of glue between operations and supply chain and the product and sales teams. We really need to be highly engaged with all of those areas. We want everyone internally to be part of our team. And we want to be the team they want to work with.

Our goal is to make customers happy and to create the ultimate customer experience. At QIAGEN you need to remain extremely engaged with colleagues all around the world in all different times zones from all different cultural backgrounds. Every day, we strive to form highly effective global teams.

In the job, you can sometimes get sucked into the day-to-day, but I think at the end of the day, we're lucky to get to take on new challenges and maintain a strategic focus. We are lucky to be driving huge improvements in people's health and in molecular biology. I think that's the overarching motivator. Because what you do is visible to the very highest level and is truly seen, and that makes you really care about the details of what you're doing."

### MATHEW ANDERSON

holds a bachelor's degree in biological sciences.

He joined QIAGEN in 2015.

Director, Head of Digital Business

Solutions QIAGEN, San Diego, CA, U.S.



## >1,880

staff in QIAGEN's commercial operations department engage day to day with our 500,000 global customers, consistently striving to exceed their expectations.

# QIASYMPHONY: FASTER, EASIER, MORE EFFICIENT

— With the placement of the 2,000th QIAsymphony system, QIAGEN reached a major milestone in the development of one of our flagship automation systems. We talked to one of our customers in Fife, Scotland, about automation to find out what makes the QIAsymphony and QIAGEN's support indispensable to them.

The imposing gray and white building of Victoria Hospital, a 452-bed NHS hospital in Fife, Scotland, is located where the river Forth meets the North Sea, just a short ride over a bridge to Edinburgh. The hospital supports all of the mid-size town, which has a population of around 365,000. It supplies services to the acute division, to the general practioners' division, and handles a number of molecular tests, including respiratory multiplex and noro virus tests that demand fast results to stop infections from spreading. Recently, the hospital installed a QIAsymphony. We met with lab managers, decision makers and scientists to talk about their experiences using the system.



## >2,000

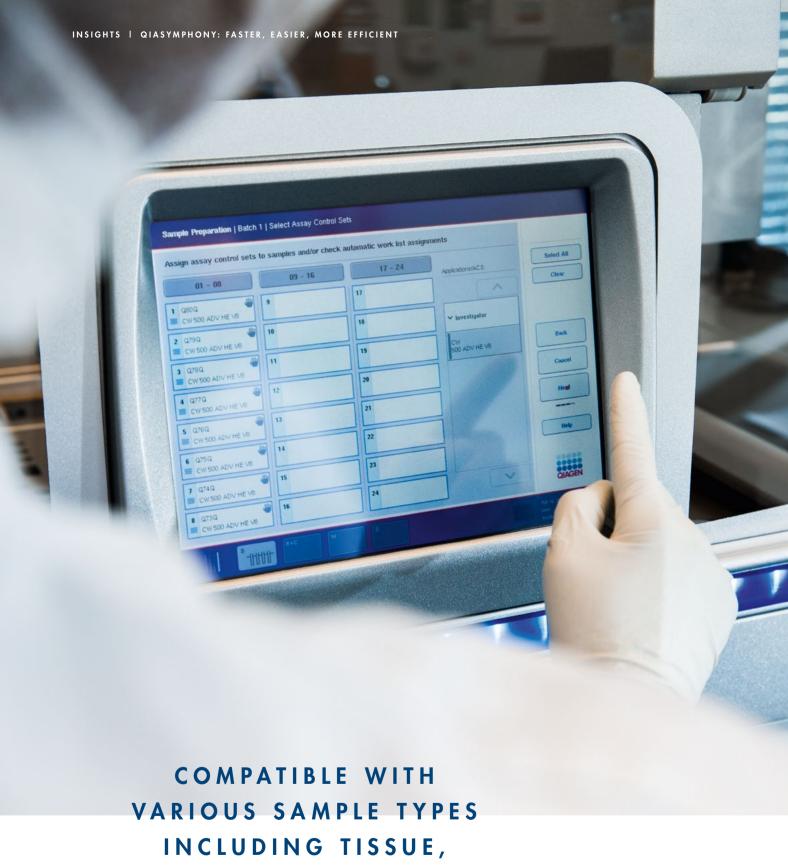
INSTALLED SYSTEMS
WORLDWIDE
AT THE END OF 2017



BOB JONES
BMS Professional Manager,
Victoria Hospital, NHS Fife,
Scotland

### QIAsymphony: one platform for many assays

"With consolidation in mind, we had to look at a solution for the assays we perform. We wanted to see if anybody could cover our assays with one platform, or maybe even two. We couldn't really find anybody that brought it down to the one single media platform like the QIAsymphony with the Rotor-Gene to actually do all the work for us. QIAGEN was a company I'd heard of. I was aware of them for a few years but I didn't actually have any experience using them or spoken to anybody who uses them. We decided: 'Let's bring it in and give it a go. If it does what it says on the package, then very good; if it doesn't, then we'll look elsewhere.' But it's done what is says on the package."



ARIOUS SAMPLE TYPES
INCLUDING TISSUE,
FFPE SAMPLES, BODY
FLUIDS, SWABS AND
CELL CULTURES



http://bit.ly/NHS\_Fife http://bit.ly/QIAsymphony





### Strategic lab consulting: ensuring a smooth workflow

"The strategic lab consulting group came into our laboratory to help us with the workflows, comparing our old existing one with the new potential workflow with the QIAsymphony and the Rotor-Gene. So we took one of our assays, the chlamydia and gonorrhea assay, and we worked through that step-by-step, in minute detail, comparing all the steps in the old process to those in the new process. We ironed out any areas where there might have been wasted time, and any benefits the QIAsymphony workflow would give us. It was a very positive experience, and at the end of that, it demonstrated that the QIAsymphony was the correct way for us to go. All the steps that we noticed that were added value with the QIAsymphony we would then implement with the rest of the assays in our repertoire."

### QIA symphony can help control costs

"Obviously finance is always a key element in providing a competitive and economic service. We have benefits both in terms of the competitive pricing offered by QIAGEN and in the fact that we are saving costs on consolidation of platform so that we don't have multiple service contracts across the board."

STEPHEN MCGLASHAN Microbiology Service Manager, Victoria Hospital, NHS Fife, Scotland



## 3

MODULAR COMPONENTS:
QIASYMPHONY SP FOR SAMPLE
PREPARATION, QIASYMPHONY AS
FOR ASSAY SETUP, AND
ROTOR-GENE Q FOR REAL-TIME
PCR DETECTION



DR. MAIRIEAD MACLENNAN
BMS Professional Manager
(Quality and Training)
Victoria Hospital, NHS Fife,
Scotland

### QIAGEN's support helps build an engaged and competent staff

"Suddenly we realized that we actually had a pretty complex setup. We filled the lab with, in total, five different setups to carry out and deliver our molecular repertoire. But we could not get a critical mass of staff trained within a reasonable period of time. With just a very small core of staff it was unsustainable. The question was: How could we deliver our services at the level that we had established?

This was the first time I'd been so closely involved with a company that was in partnership with us to achieve our goals, a very refreshing and new approach for me. Right at the beginning, my priority was the training. To have a system to train more people on, more efficiently, and maintain and monitor their competence in how the system looks, how could we absorb that into our existing training procedures, and how we would prepare the documentation.

We couldn't have actually managed that without the input of QIAGEN staff, who provided us with documents and background information about the platform, with information about their internal training procedure – about the whole methodology of training on the QIAsymphony and Rotor-Gene system. We didn't have to write anything from scratch, which is always a big fear because it turns into such a big operation that you'll lose objective. They also provided us with excellent quality documentation, which was very easily captured in our own system."



"I don't view having a quality outlook as obsessive perfectionism, but more as putting forth my best effort, going the extra mile to meet a need, striving to improve, and honoring commitments in my personal as well as professional life.

At QIAGEN we strive to actually exceed standards and our customers' expectations. Customers depend upon us to provide the best solutions possible. QIAGEN products are renowned for their quality and reliability – we're committed to these values. When there is a problem, and occasionally there is, we in the quality organization are an integral part of the solution.

If something seems like it's not quite right, everybody from the person working on the line to the person taking a customer's call is not afraid to bring it up, and we work together to correct it. There is no fear of saying, "This might be wrong." I've always received full support from the very top level of the organization. Without that support, it would be impossible to create an environment where the highest quality is part of everything we do. We really live it."

#### **DONNA SOWERS**

holds a bachelor's degree in biochemistry.

Donna joined QIAGEN in 2003.

Senior Director QA Product Quality Operations,

Germantown, MD., U.S.



# >1,080

highly qualified employees in QIAGEN's operations team work relentlessly to provide the highest quality Sample to Insight solutions designed to meet even the most critical requirements of modern research and diagnostics laboratories.

## ON A MISSION

— QIAGEN is advancing sustainable business practices in line with its vision to make improvements in life possible. QIAGEN's efforts reflect our belief that various dimensions such as social and employee matters, diversity, respect for human rights, anti-corruption, and environmental issues are interlinked and reinforce each other.

Sustainable business practices have been part of our DNA since the beginning. As a market and innovation leader in life sciences and molecular diagnostics, we strive to go above and beyond simply following requirements of environmental and labor laws. There is much room for innovation in driving sustainable development in our industry, and we are resolved to continue to move forward.

The scale of our ambitions brings us together with many important partners all over the world. One example is our collaboration with the Clinton Health Access Initiative (CHAI) that aims to improve access to cervical cancer screening in Africa using our careHPV system. Together with the international health organization PATH, and with support from the Bill and Melinda Gates Foundation, QIAGEN specifically developed careHPV for use in low-resource settings.

#### **Clinton Health Access Initiative**

The foundation's goal is to provide access to healthcare for millions of residents in low- and middle-income countries. Today, CHAI operates in 33 countries across the developing world that account for about one-third of the world's population, and more than 70 countries are able to access CHAI-negotiated price reductions for drugs, vaccines, medical devices and diagnostics.

Ira Magaziner, CEO at CHAI: "HPV plus cervical cancer is still a death sentence in remote areas in Africa. With an extensive series of tests, we want to implement a screen and treat campaign."

### "A GOOD DIAGNOSIS IS KEY."

DR. CATHARINA BOEHME,
CEO at FIND, talks about reverseengineering, the odds of adequate
treatment and FIND's cooperation
with QIAGEN

You have worked in global hotspots. Can you share your observations?

DR. CATHARINA BOEHME In Africa we often had to watch helpless people die, without even knowing what they were suffering from. For instance, 60 to 95 percent of children with a negative malaria test will receive antibiotics despite only 10 percent of these children needing them. The situation with tuberculosis is similar. Access to efficient diagnostics is prerequisite to combat infectious diseases – without that we lose too much time, treat with the wrong drugs and, as a result, the costs are too high.

Which diseases cause the most concern?

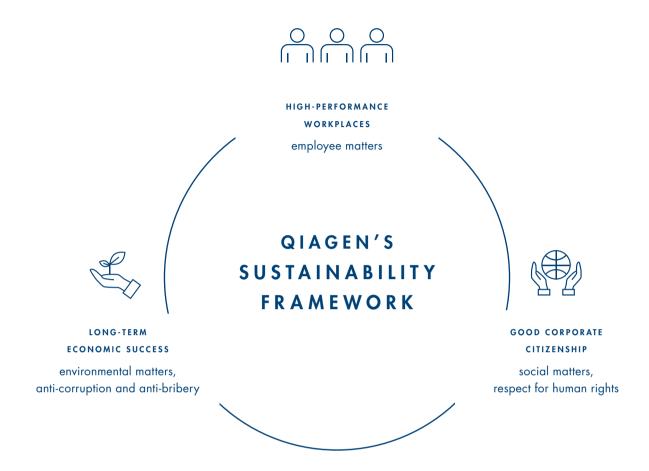
In some countries we count more deaths from Hepatitis C than from HIV. Often this disease is diagnosed in but a very small percentage of people.

Which approaches does FIND pursue?

We carry out screenings in high-risk areas, for example in drug addicts living in slums. Here, dangers lurk even in medical facilities, because blood transfusions are contaminated. A good diagnosis is the key to success in fighting infectious diseases.

But diagnostics costs money and require the presence of a basic healthcare system. Which challenges do you face? We need to downgrade high tech for low-tech applications. In the case of sequencing technologies, that means an easy-to-use, robust basic version is created from the high-tech product. It's called reverse engineering. In certain cases we can replace liquid testing with these pared-down sequencing technologies. The doctor immediately has a result, but above all, a laboratory is not necessary. In remote areas, that's not trivial.





QIAGEN also aims to advance TB diagnostics to help reduce the global burden of this deadly disease. Our partnership with FIND spans three areas: tests to enable targeted preventive therapy, tests to detect drug resistance at the point of care, and sequencing as a future gold standard in TB surveillance and regimen selection. We also work on improved tests to detect patients with latent TB who are at risk of active disease progression.

These are just two concrete examples of how QIAGEN delivers on our pledge to make improvements in life that will last. To learn more about our activities related to various dimensions of sustainability and the progress we make, please visit our website at <a href="http://corporate.qiagen.com/about-us/Sustainability/overview">http://corporate.qiagen.com/about-us/Sustainability/overview</a> or read our Financial Report online at <a href="http://financialreport.qiagen.com">http://financialreport.qiagen.com</a>.

#### FIND

An international nonprofit organization based in Geneva, Switzerland, that enables the development and delivery of much-needed diagnostic tests for poverty-related diseases

## THE DNA PROFILER

— DNA profiling has become routine practice in criminal investigations. QIAGEN is helping forensic specialists around the world solve even the toughest cases with high quality analysis of hundreds of thousands of samples a year. Here is a look at some of our activities in North America and the U.S. – science can be thrilling.



#### Investigator 24plex QS Kit

In January 2017, the U.S. Federal Bureau of Investigation (FBI) mandated that DNA "STR" profiling be expanded to a core set of 20 markers. QIAGEN's Investigator 24plex kit – our flagship DNA profiling assay – meets this new requirement and has been adopted by a number of laboratories across the United States.

Bode Cellmark Forensics; Bureau of Forensic Services, Pennsylvania State Police; Alabama Department of Forensic Sciences

#### QIAsymphony

Labs like Bode Cellmark Forensics process many thousands of samples annually and face the challenge of achieving this throughput without compromising on sample quality or DNA profile success rates. The QIAsymphony has proven to be the instrument of choice for labs wishing to replicate their manual success rates in a high throughput setting.

U.S. Army; San Diego; New York State; Florida Department of Law Enforcement

#### EZ

Purification of DNA from casework samples requires a high rate of recovery of pure DNA. This is uniquely challenging in that the samples typically contain very little DNA. In addition, they are frequently contaminated with substances such as dirt or clothing dyes that impair downstream processing. The EZ1 is established as the most popular choice for automation of the sample purification process due to its speed, DNA yield and purity, as well as flexibility.



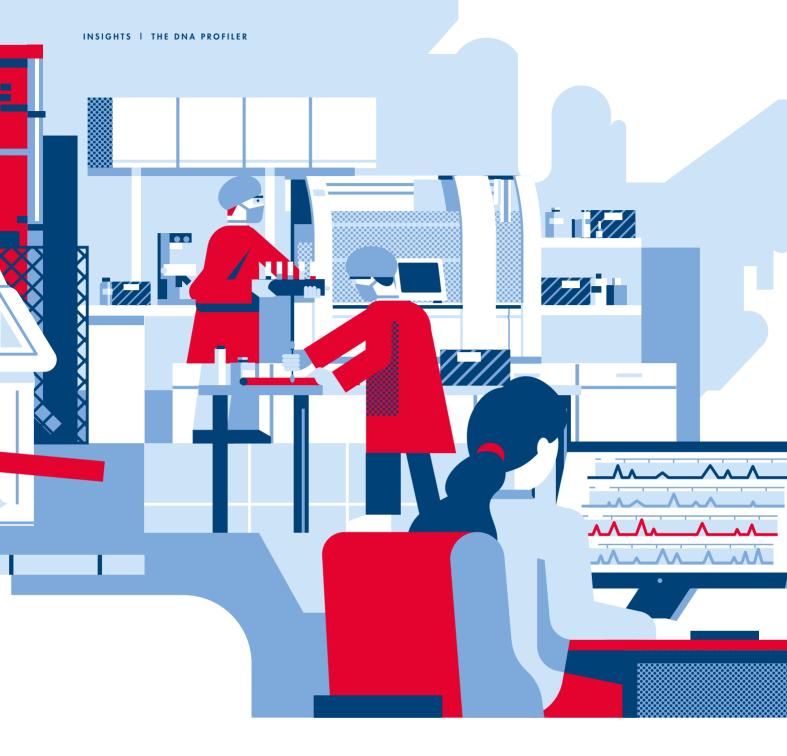


http://bit.ly/QIAGEN\_HID

FBI; Florida Department of Law Enforcement; Houston Police Department

#### **QIAcube**

The QIAcube is the only platform in HID (human identification) which is able to automate the samples required for analysis of sexual assault evidence. It involves the physical separation of spermatozoa from the victim's cells. This is typically achieved by using centrifugation followed by careful pipetting, a time-consuming process that has resulted in sample backlogs in many labs across North America and globally. The QIAcube enables laboratories to process samples in a streamlined manner, reducing backlogs and enabling the identification of perpetrators who would otherwise remain unidentified.



#### U.S. Army; North Carolina State Crime Lab; Louisiana State Police

#### **QIAgility**

Numerous labs now choose the QIAgility to automate pipetting steps to ensure reproducible and accurate pipetting and successful assay setup like with QG. DNA profiling workflows require numerous pipetting steps as PCR assays are set up and samples are prepared for capillary electrophoresis. QC automates these time-consuming and error-prone steps.

#### Verdugo Regional Crime Lab, Glendale, CA; Santa Clara Crime Laboratory

#### **Validation services**

Forensic validation can be work-heavy and requires experienced scientists. QIAGEN's North American forensic team offers validation services to facilitate a faster and easier adoption of new QIAGEN products into customers' workflows.

#### **Royal Canadian Mounted Police**

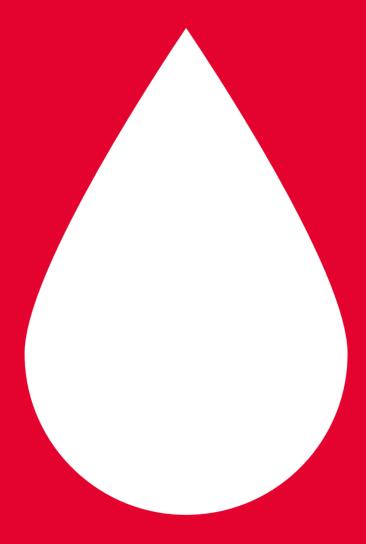
#### **Quantiplex HYres Kit**

Quantification of purified DNA is essential to ensure the optimal performance of DNA tests on valuable, limited casework samples. QIAGEN's quantification kits are uniquely designed to offer the most sensitive quantification and the most informative data on the quantity and quality of sample DNA, ensuring the best possible chances of downstream success.

# CANCER-ID

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Imagine identifying individual risk for a specific cancer, detecting a tumor not yet visible, profiling tumors to personalize therapies or closely monitoring treatment to ensure the best possible outcomes for patients – and all of that just by analyzing simple blood samples.

In working with the 2015-formed European consortium CANCER-ID, funded by the Innovative Medicines Initiative (IMI), QIAGEN is helping to bring the tremendous promise of liquid biopsies into routine clinical practice.



#### "LINKING RESEARCH AND PRODUCT"

#### As an academic, what do you expect from collaborative research with industry partners?

Cooperating with industry players creates an important link between scientific publications and products. For instance, there are a number of academic research programs for biomarkers, and a few thousand have certainly been published, but there are still too few diagnostics that have reached the clinic.

#### What exactly does CANCER-ID do to create that link?

It's not about developing new products but testing well-known biomarkers and the corresponding technologies such as liquid biopsy. Very few of the currently available products are certified, so we doctors don't always know exactly when to best use which product.

#### Which personal goals do you hope to achieve?

I've worked as a scientist for more than 30 years, collecting achievements, publishing numerous papers, being able to do research at a first-class university – and yet my scientific career would be a personal disappointment if none of it led to products that improve patient care. In this light, liquid biopsy is a great step for cancer patients: it's a less harmful and a potentially more effective tool. It combines the needs of all stakeholders: aiding physicians in making better decisions, helping healthcare systems to become cost-efficient and improving outcomes for people suffering from cancer.

#### PROF. DR. KLAUS PANTEL,

head of the Institute for Tumor Biology at University Hospital Eppendorf in Hamburg, Germany, is a pioneer in the field of cancer micrometastasis, circulating tumor cells, and ctDNA PARTNERS COUNTRIES UNIVERSITY MEDICAL CENTER BAYER AG HAMBURG-EPPENDORF this public institution plays the pharmaceutical company serves as the main a major role as a co-coordicoordinator of the nator of the consortium. CANCER-ID consortium. CANCER-ID is supported by the Innovative Medicines Initiative (IMI), a joint undertaking under Grant Agreement No. 115749. The project is financed by the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies' in-kind contributions. http://www.imi.europa.eu/projectsresults/project-factsheets/cancer-id

€16,523,092

Total CANCER-ID budget, contributed by the IMI and project partners

# 1 GOAL BEATING CANCER

#### JOINING FORCES TO DEFEAT CANCER

Public and private institutions, major players and mid-sized companies, academics and clinicians are joining their considerable forces to fight cancer. The 38 members of the CANCER-ID consortium have one mission: to identify and establish the clinical validity of novel blood-based biomarkers for cancer and establish protocols for the processing of the corresponding samples. Their work aims to improve treatments and outcomes for cancer patients. Their mode of operation: working tirelessly, collaborating and communicating across borders. In addition, feedback from regulatory agencies (EMA/FDA) and patient advocacy groups like Mammazone is taken into account by the project, coordinated by the University of Hamburg, University of Twente, Bayer AG and Menarini Group. QIAGEN, a pioneer in the field of liquid biopsies, announced in 2017 that it had joined the consortium to support the standardization efforts with its technologies and expertise. QIAGEN is the only company providing basic and clinical researchers with Sample to Insight solutions for all three emerging liquid biopsy approaches: circulating cell-free nucleic acids, circulating tumor cells and exosomes.





About five to 10 milliliters of blood, equal to about one to two teaspoons, are needed for a liquid biopsy. Currently, the potential of liquid biopsies is explored for several different cancers, including lung, colon, breast and prostate.

#### POTENTIAL BENEFITS





WHO IS AFFECTED?

WHAT IS THE BEST TREATMENT?

Liquid biopsies hold great promise for the development of novel screening approaches to improve the early detection of cancer by identifying tumors long before they can be diagnosed using traditional imaging tools.

Liquid biopsies can help to characterize a tumor's molecular makeup to determine the best therapy for a patient when a tissue sample is not available. They can also help healthcare professionals to cope with the issue of tumor heterogenity.

## THE ULTIMATE GOAL

Liquid biopsies rely on the detection of small particles shed by a tumor in the blood. These include circulating tumor DNA (ctDNA), microRNAs, circulating tumor cells (CTCs) and exosomes. These molecules can be isolated, compared and their identity verified. Their composition is representative of the patient's tumor – and a door-opener to novel approaches for the detection, profiling and treatment of cancer. The ultimate goal: to help more patients and defeat the deadly disease.



CIRCULATING TUMOR DNA (ctDNA)

originates from dying tumor cells and represents the genetic diversity of the total tumor burden in the body. ctDNA can help to predict therapy resistance or success.



CIRCULATING TUMOR CELLS (CTCs)

are intact cells separated from solid tumors into the bloodstream. They are potential seeds for metastasis and contain the tumor's genetic and expression profile – thus providing the most detailed insights into its molecular profile.



EXOSOMES

are microvesicles actively shed by tumor cells. Exosomes contain tumor RNA and can give insights into its expression profiles, providing valuable information for treatment decisions.



WHO WILL RELAPSE?

Numerous studies have shown the potential of liquid biopsies in tumor staging. Also, liquid biopsies can assist in post-surgical surveillance of minimal residual disease and enable the identification of patients at risk of recurrence.



HOW WELL IS THE TREATMENT WORKING?

As minimally invasive procedures, liquid biopsies can help healthcare professionals to closely monitor cancer patients, helping to assess the success of a therapy and anticipate emerging therapy resistance.

# 5 PACKAWITHIN

To make a project of these dimensions go smoothly, CANCER-ID is carefully orchestrated and divided into five parcels, so-called work packages:

#### WPO // Technology assesment

The first package has four major objectives: Evaluating criteria for CTC technology and analyses of circulating nucleic acids, establishing clinical-ready protocols and a data management and sample storage strategy.

#### WP1 // Lung cancer

In lung cancer, the researchers work on methods to count and characterize CTCs, and the analysis of plasma nucleic acids. These results are checked and confirmed in a number of clinical studies.

#### WP2 // Her2-therapy resistant breast cancer

In breast cancer, the antibody drug trastuzumab has dramatically altered the lives of HER2-positive patients. Finding a way to identify patients who are or will eventually become resistant to this drug may open the door to new treatment pathways.

#### WP3 // Data management & bioinformatics

Harnessing and learning from the reams of data created throughout all stages.

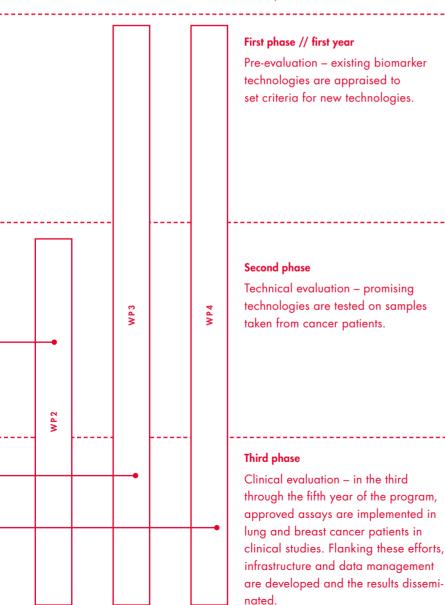
#### WP4 // Project management & dissemination of results

Making sure everything runs smoothly and insights are made available to key players.



## AGES 3 PHASES

The project is spread over three phases:



#### "TACKLING FUNDAMENTAL QUESTIONS"

#### For CANCER-ID, companies cooperate instead of competing – does that work?

Yes, because it is a project on a precompetitive research level, tackling fundamental questions that can't be solved by a single company or university alone.

#### Where do you see liquid biopsy's potential?

First, monitoring – as soon as we pick up weak signals in the blood, we can change or adjust treatment early. Second, minimally invasive applications for very ill patients who have been taxed by multiple therapies. Third, a heterogenous look at the tumor – we can show the growth of metastases and depict all information for the residual tumor. With a tissue sample, we can only see the data that a single section delivers.

#### What motivates you personally?

I want to decrease the patient's burden and increase the prospect of a successful treatment. In addition, the interdisciplinary work excites me, especially the cooperation with the patients' groups. It shows us what we work for, and how much of that actually reaches patients.

#### DR. THOMAS SCHLANGE,

senior biomarker scientist at Bayer AG and a chemist by training, is the coordinator of CANCER-ID on behalf of companies belonging to the European Pharmaceutical Federation Industry Association (EPFIA)



# THE INCREDIBLY TALENTED ALPHABET OF LIFE

— With the age of biology no longer in its infancy, scientists are finding an ever growing number of uses for DNA. Here are some of the applications of the ultimate molecule that were unthinkable even just a few years ago.

# d

#### Teddy bear-shaped cavity

DNA is a powerful medium, transporting the very blueprint of life from generation to generation. But its pliable, tentacle-like strands also make for a robust and self-assembling building material – at least in nanostructures. Last year, scientists found ways to build bigger DNA-origami structures. They used inspiration from fractals, step-wise construction and DNA bricks to build more complex and larger structures, including a cube with a teddy bear-shaped cavity, a dodecahedron and a self-assembled rooster.

8,700

pixels measuring 0.5 micrometers a side was the size of a DNA-origami based image of the Mona Lisa.

#### The smallest pair of tweezers

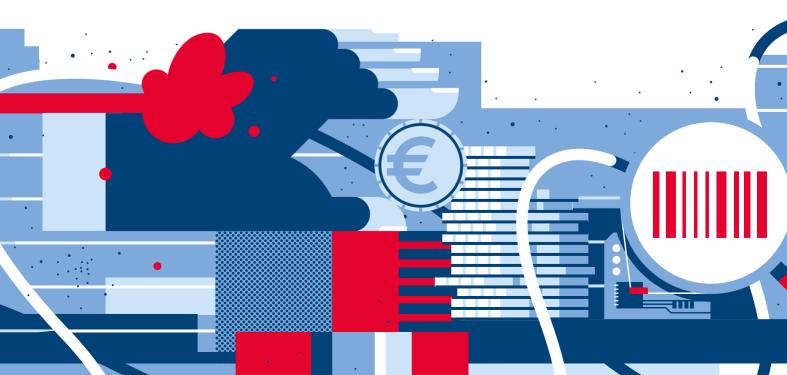
Mother Nature excels at building nanomachines. Take, for example, flagella, the whiplike structure that allows cells to move. Now humans are, slowly perhaps, making the tiniest of machines. Here again DNA is used as a self-assembling building block, not as a carrier of information. Scientists have built nanowires and small devices, as well as the tiniest pair of tweezers. Maybe someday a nanorobot will navigate human bodies to deliver drugs or repair damaged tissue.

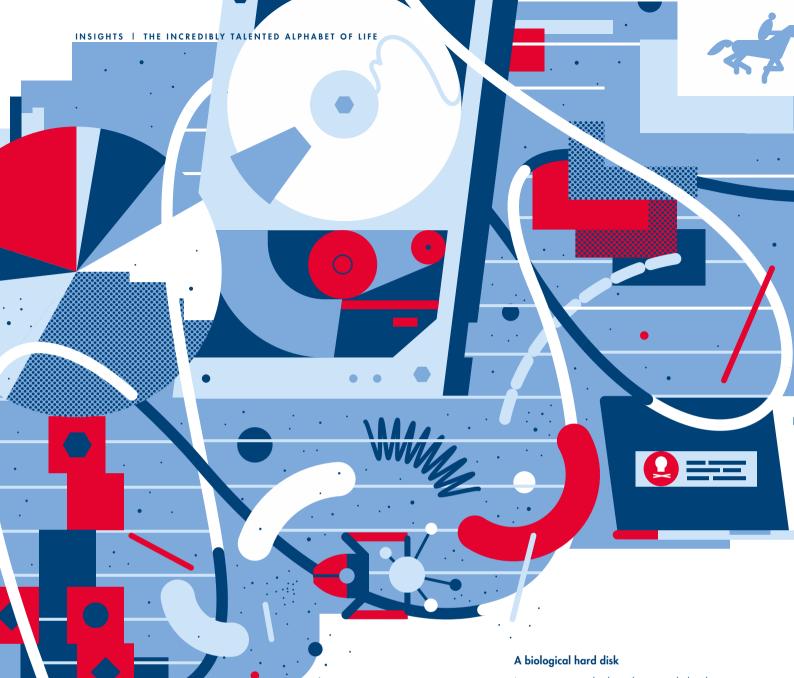
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Nanometers was the length of a DNA robot stride researchers at the prestigious California Institute of Technology built to transport specific molecules.

#### Gotcha!

We all know that a criminal's DNA - in the tiny amounts of skin a person continually sheds or in a wisp of hair - can reveal their identity to the police. Now, a number of businesses are offering a novel take on DNA identification: Through the push of a hidden button, a fine mist of synthetic DNA is sprayed on, say, a thief trying to rob a bank or steal money from a cash register. The tiny amounts of genetic information are not easily washed off, and irrevocably place a perpetrator at the scene of a crime. A similar approach is being used to combat supply chain fraud, especially counterfeit electronic parts in the military. Here a DNA solution is sprayed on the parts in question. Holding them under a special light causes the DNA to glow, ensuring that it's been tagged. A more thorough scientific examination of the DNA can be used to track the com-





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years after the first "movie" shown on the screen comprised moving images of a running horse, scientists under the direction of Harvard geneticist George Church uploaded the equine film into the DNA of E. coli by using CRISPR/Cas9 technology. The animated Gif was screened after it was recovered by sequencing the bacteria's genome.

#### **400 BILLION**

gigabytes of data can be stored in 1 gram of DNA – theoretically. In our increasingly data-driven and cloudbased world, a biological material like DNA might seems anachronistic as a way to store data. But DNA's value as a data storage medium has been known for more than 70 years, since Erwin Schrödinger proposed a hereditary code-script that could be loaded into a structure he described as an aperiodic crystal. Today, a new way of data storage is a pressing need. Note, more data were created in the past two years than in all of history before. A flood of data that soon may surpass hard drives' ability to capture it. Microsoft already plans to have an operational storage system based on DNA toward the end of this decade.

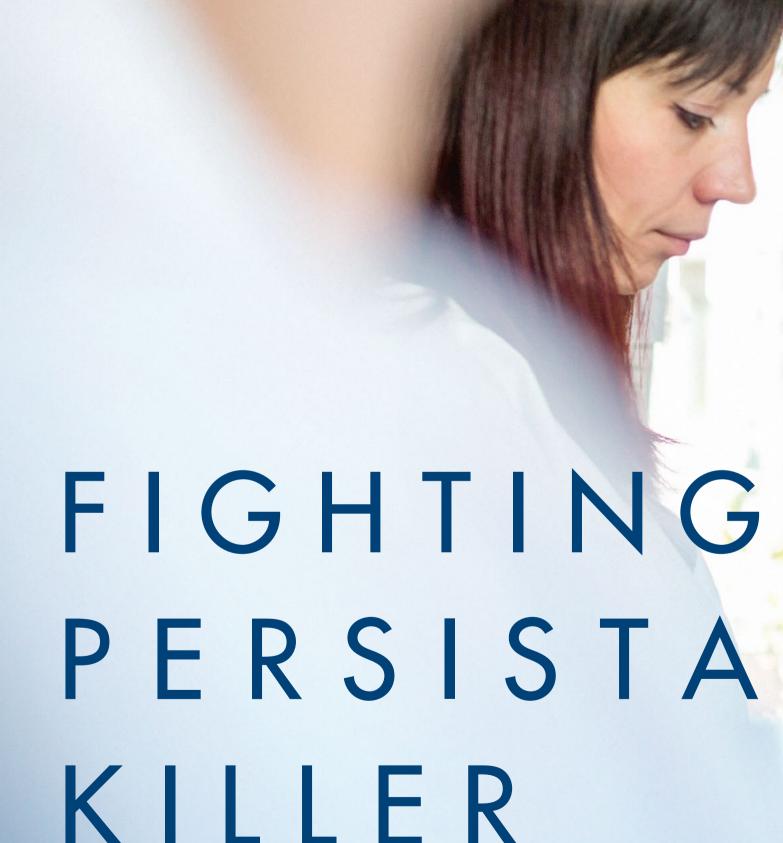
take over the supporting IT infrastructure, as scientists from the University of Washington have shown.

Isn't it ironic? A computer virus

can be encoded by DNA. As

the encoded program can

soon as the DNA is sequenced,





— Tuberculosis is one of the oldest infectious diseases – and still one of the deadliest. Scarce funding threatens to hamper its eradication and has given rise to the threat of multi-resistant strains that demands new approaches in fighting the disease. QIAGEN starts this fight with its QuantiFERON technology – considered to be the most accurate test for TB infections.

uberculosis has reclaimed a spot among the top 10 killers globally. About 1.7 million people succumbed to it in 2016, according to a World Health Organization report. The main factor that keeps tuberculosis around is that scientists still don't understand what happens between the moment the bacterium enters the body and years or decades later – the disease wakes up or reactivates.

Available tests are currently only approved to detect two stages of the disease: latent tuberculosis infection (LTBI) and active disease (TB). A diagnosis of active TB usually requires a microbial culture and an x-ray or a biopsy if the disease affects organs besides the lungs. As for latent infection, the tuberculin skin test (TST), or Mantoux, has long been the most common way to detect it. But the century-old test has several disadvantages: it requires two visits to the doctor and its interpretation is highly subjective and error-prone. In addition, it can't distinguish between an infection or a previous vaccination with bacillus Calmette-Guérin (BCG).

#### The most accurate test

In the early 2000s, a new laboratory blood test reached the market. Called QuantiFERON, it requires mixing some of the patient's blood with Mycobacterium tuberculosis protein fragments. The level of the immune response in the blood sample is used to determine if the patient's immune system knows the bacterium from a prior TB infection.

#### 1.7 million

Deaths total more than AIDS, far more than malaria, disproportionately more than Ebola. And despite efforts to curb the epidemic, there were more than 10 million new cases worldwide in 2016.

#### Years or decades later

According to recent estimates, up to one-fourth of the world population has a latent TB infection – a state during which the bacteria remain dormant and do not cause any symptoms – and only 5 to 10 percent of these individuals develop active TB, often long after the infection.

#### BCG

Though the BCG vaccine is no longer common in Western countries since it offers only limited protection against adult TB, it is still the most common vaccination in the world. In Africa, almost everyone gets vaccinated within the first week of life and protects infants from disseminated tuberculosis.





Every day, the translational research unit at Italy's National Institute for Infectious Diseases (INMI) receives and processes several blood, urine and broncholavage samples taken from patients in different stages of tuberculosis infection or disease.

#### "OUR GOAL IS TO DEVELOP EASY AND QUICK TESTS"

Dr. Delia Goletti is fighting TB at Italy's National Institute for Infectious Diseases (INMI) in Rome and took part in enhancements of QuantiFERON

DR. DELIA GOLETTI

heads the Translational Research Unit

at INMI, which she joined in 1999.

She started off as an HIV researcher.

After graduating medicine in 1990, she

studied how the immune system is

affected by HIV, and spent four years

at the National Institutes of Health in

Bethesda, MD, in the laboratory

directed by Dr. Anthony Fauci before

returning to Italy.

Dr. Delia Goletti heads a laboratory team of seven and sees about 15 patients a week in the outpatient clinic. INMI is the reference center for tuberculosis in central and southern Italy, and takes in about 300 cases a year (mostly immigrants) including rare cases of drug-resistant TB. Goletti's lab is also working with Professor Gian Maria Fimia's group from the University of Salento, in Lecce, Italy. Their work shows that tuberculosis inhibits autophagy, the process by which a cell gets rid of unnecessary particles and also controls the replication of bacteria. TB is not a new germ, like HIV was in the 1980s or SARS was two decades later. On the contrary, the disease has been around for as long as mankind, and the bacterium at its root has been known for more than a century. It does not spread as easily as measles, rubella or influenza, but without treatment, drug-resistant TB has a mortality rate that is similar to Ebola's.

#### What makes it so difficult to defeat, Dr. Goletti?

There are different reasons. Good socioeconomic conditions are the best defense against Mycobacterium tuberculosis, the bacteria that causes TB. That is why the infection thrives in developing countries where malnutrition weakens the immune system of the poorest people. In most developed countries, improved nutrition and hygiene were enough to turn tuberculosis into a rare disease by the early

1950s. Which, paradoxically, led to a second major problem: wealthy nations shifted their attention away from TB to other health issues.

#### Which was a mistake?

When I was in Bethesda, Maryland, at the National Institutes of Health, we realized there was a new epidemic due to co-infection with HIV. By turning off the immune system, HIV paves the way for tuberculosis, which, in turn, helps HIV replicate faster. About 400,000 people a year die from co-infection with HIV and TB. This also affects wealthy nations; furthermore, as life expectancy grows, there are more and more things that can weaken the immune system in addition to the natural aging process and unleash the disease, for instance therapies for autoimmune disorders or diabetes.

#### How does one tackle that problem?

Our goal is to develop easy and quick tests that can tell who has a dormant infection, who is progressing toward the active disease, and who has active tuberculosis. Working with the latest version of the QuantiFERON test, the QFT-Plus, we can, besides CD4 T-cells, also measure the CD8 lymphocyte reaction. We've been looking for antigens that cause a reaction only during the disease, as well as antigens that only show up in latent infections. And we've been experimenting with different readouts, test formats, biological samples – for example, using urine instead of blood.

#### Could that insight lead to new therapeutic strategies?

By better understanding this process it might become possible to stage the disease and spot at-risk subjects. This may open

up new therapeutic strategies. It may be possible to use candidate "antigens of latency" as Rv-2628, a protein that Mycobacterium tuberculosis produces when it is starved of oxygen, as happens during latent infection.

#### How did you find that out?

When measured in blood samples, this antigen provokes a much lower response in sick patients with TB than in those simply infected. More important, it seems to offer a way to date the infection. It may be

an important discovery because recently infected patients are considered at higher risk of developing the disease.

#### Are other breakthroughs likely to come?

Very interesting seems analyzing gene expression profiles of LTBI patients. Early study results conducted in South Africa suggest that patients who are progressing to active disease, exhibit a specific 16-gene signature which could be used to identify those at risk and reduce the number of unnecessary treatments. While this approach still must be validated in larger clinical studies, it holds great promise for the development of novel predictive tests to improve the management of LTBI infections.



Dr. Delia Goletti is fighting tuberculosis at INMI in Rome and one of the "early users" of QuantiFERON technology.

#### **QFT-Plus**

QFT-Plus includes two test tubes: one equipped with antigens that provoke an isolated CD4 response, and one in which both CD4 and CD8 reactions take place. Its main clinical application remains the indirect test for M. tuberculosis infection, as the previous test.



www.inmi.it www.QuantiFERON.com The QuantiFERON technology, unlike TST, is not fooled by previous immunizations and is considered to be the most accurate test for TB infection.

Since QuantiFERON was brought to market, more than 40 million tests have been done with the technology. Dr. Delia Goletti had been one of a few scientists worldwide who could test the latest assay version as "early users" already two years before it entered the market. Her research at Italy's National Institute for Infectious Diseases (INMI) in Rome contributed to the fourth generation of the QuantiFERON test, QuantiFERON Gold Plus (QFT-Plus).

Previous versions only measured the activity of CD4 T-cells. But factors, such as the HIV virus that directly kills CD4 T-cells, impact all tests that measure CD4 immune responses. The latest QuantiFERON test also detects a CD8 lymphocyte reaction. These "killer cells" attack the bacterium reducing their growth.

## 40,000,000

## TESTS HAVE BEEN DONE WITH QUANTIFERON, SINCE THE TECHNOLOGY HAS BEEN INTRODUCED TO THE MARKET

#### **HIV-TB** co-infection

A recent study in a Zambian TB clinic showed that QFT-Plus sensitivity is not affected by HIV status except in patients with severe immunosuppression.

#### WHO's goal

The WHO's global target is to reduce tuberculosis cases to just one per million inhabitants by 2050 – a 50-fold reduction.

#### Unnoticed

Infected at a young age, humans can keep the bacterium in their system up to 60 years.

Research indicates the test may potentially be suitable for patients with weak immune systems, in particular in patients with an HIV-TB co-infection. Historically, reliably diagnosing a TB infection in this group has been challenging because their CD4 reaction is frequently suppressed. Goletti's group has also proven that a higher CD8 response is strongly associated with active and severe TB. The test's CD8 response is strikingly different for mild or severe disease. Active disease and severe cases lead to significantly stronger CD8 reaction than mild tuberculosis disease; this response decreases after treatment. Which means that, as a Japanese study has recently suggested, QFT-Plus might potentially be used to monitor treatment efficacy.

#### Reaching the goals

With new biomarkers and approaches to better understand TB, the WHO's goal of an 80 percent reduction in cases and a 90 percent reduction in related deaths by 2030 is in reach. Most of the work will have to be done in developing countries – in particular, India and South Africa, but also Indonesia, China, Nigeria and Pakistan. But richer countries cannot afford the luxury to keep neglecting TB. The ability of TB infection to go unnoticed for years makes it an ever-present factor. And as life expectancy grows, there are more and more causes that can weaken the immune system and unleash the disease: biologic therapies used for autoimmune diseases, diabetes, or simply old age.

For those reasons an accurate test has outstanding importance. It will enable a more exact staging of the disease, increasing the chances of beating tuberculosis.



"I've always been fascinated by new technologies. Personally and professionally, I think it's not always about finding something absolutely new, but rather about never standing still and regularly reinventing oneself.

Our goal in the Digital Lab is to develop ideas for new digital business models that can help us as a company to grow and transform. We help identify opportunities, create concepts, and initiate their realization.

To fill the idea funnel, I routinely look for new developments where digital technologies like virtual reality, artificial intelligence, blockchain or data-based business models are used in our industry and beyond. I frequently screen key information sources like tech blogs, startup news or industry reports and speak to experts in the digital ecosystem.

My biggest personal wish is to grow very old so that I can experience all the fantastic developments that are certain to become reality in the decades to come."

DR. ALI MURAT KAYA

holds a Ph.D. in neurobiology and joined QIAGEN in 2017. Digital Innovation Manager, Hilden, Germany



> 60

members of QIAGEN's Digital Accelerator are dedicated to drive innovation across the company's entire value chain – ultimately aiming to enhance customer experience.

# PROMISIN FUTURE

\_\_\_ Dr. Richard K. Wilson, executive director of the Institute for Genomic Medicine at Nationwide Children's Hospital in Columbus, Ohio, has helped drive genomic discoveries and medicine since the 1980s. He reflects on advances in molecular medicine and how interpreting genomic findings will increasingly inform diagnosis and treatment decisions.

Rapid progress in genomic science has changed the way we look at the human body, health and disease. Dr. Wilson, you have been a hands-on participant, so where do you see the future going? If I look at where we are now, with next-generation sequencing and other technologies, I think back to when I was sitting in a lab at Caltech in about 1988 or '89 talking to Jim Watson. We all thought 'How the heck are we ever going to sequence the human genome, or even bacterial genomes, when the technology isn't there?' It took two days just to sequence 16 samples. But we had this idea where sequencing could eventually go - it was just a question of pushing the technology. Fast-forward to today: we've seen wave after wave of improvements, greatly reducing the cost and expanding what sequencing can do. That progress makes it easier to envision the future. These changes will have a tremendous impact on medicine and patients.

For example? | So I have this iPhone in my hand. I can envision some sort of device, about the size of my thumb, that plugs into the port on my iPhone that basically could take a drop of blood and sequence a human genome in relatively quick order, connect to a server and give me not only an analysis but an interpretation. It might tell us about a mutation in a particular gene, and based on the literature, we would know that the disease phenotype is likely going to be this, so a great course of treatment would be that. When we have that kind of incredibly fast, comprehensive and inexpensive technology, we'll be able to sequence the genomes of newborns routinely, and we'll be able to predict diseases on a relative schedule. As children mature into adults, physicians will know better how to care for each individual.

Do you think we're moving toward sequencing the genome of every newborn? I see no reason why that can't happen, short of simply not presently having available funds to develop the technology. Today, when every child is born they get a little 'heel stick.' The hospital takes a little blood from their heel and a small bevy of tests is run on those newborns. If the tests indicate a disorder, the pediatrician gives the parents special instructions to prevent or deal with that disorder. More and more, these are not simple biochemical tests but also look at DNA – we check for maybe 50 different heritable disorders. Once the cost goes down and we have the ability to interpret the information and pass it to physicians in an understandable manner, you could envision whole genome sequencing for every child.

When do you think this will come about?

I think we're still years from sequencing newborns in a widespread manner, but the technology is in hand. It's a question of how to lower the cost and improve our ability to scale it up. Right now at Nationwide Children's, we perform exome sequencing on selected patients and both parents. It takes a couple of months to get the interpretation – that's too slow. It also costs about \$8,000 per family. So we need to improve the technology, but we can do that. The tougher question that's going to limit how quickly this becomes routine is the healthcare funding picture.

So do you think everyone, ultimately, should have their genome sequenced? At this point, I feel strongly that the only good reason for a healthy adult to be sequenced is cancer – if I had a cancer diagnosis, I would definitely have my genome sequenced. But right now, sequencing isn't going to tell a healthy adult all that much they can use in their personal healthcare management. It would be a different story for newborns. When we have comprehensive newborn sequencing, we would pick up clues from the genome that provide advance warnings, some of which would be actionable. For patients who won't show symptoms until years later, these early clues could enable an intervention before a disease develops. I think we'll get there at some point.

How would you explain the potential of genomic information to a layperson?

I think of our genomes as sort of a human operating system, and a gene as a bit of code within that system, which might be specific to a function in a cell or a disease. You and I use computers to write, check email, read the news – and we never think about the program code that underlies what we do with Windows or Mac OS. Our genome sequence is similar to the operating system that allows us

to use a computer, and when it's bug-free, it allows us to be well. If something goes wrong, if there's a bug in the code, we may develop a disease. The cool thing is that, both for the computer and the genome, there are ways to de-bug. Once you've found the root of an error, which is what genome sequencing allows, quite often you can address it. Of course, it does take an experienced person with special skills to do that.

Are doctors ready? How do you see the use of genomic information evolving in healthcare? Clearly, as the role of genomics grows, so too does the training of doctors in molecular medicine. Many oncologists already understand that genomic testing provides one more very useful insight into a patient's disease. To diagnose a cancer patient, often there is a biopsy and cells are examined under the microscope. Examination determines the patient's physical condition, if they're relatively healthy and strong, or older with a lot of complications. Beyond these standard tests and examinations, genetic test results are seen by the physician as an additional piece of information to help determine the best treatment. A mutation in a particular gene can indicate that the patient is a good candidate for a targeted therapy. In the future, interpretation of genomic findings will increasingly inform diagnosis and decision making on treatments.



DR. RICHARD K. WILSON

executive director of the Institute for Genomic Medicine at Nationwide Children's Hospital in Columbus, Ohio, and professor of pediatrics at the Ohio State University College of Medicine, earned his Ph.D. at the University of Oklahoma, one of the first Sanger sequencing laboratories in the United States, then did post-doctoral research at the California Institute of Technology, a hub for new sequencing technologies. In his 23 years as director of Washington University's genomics institute, Dr. Wilson played key roles in the sequencing of the first animal genome, the Human Genome Project, the first study to sequence the genome of a cancer patient and discover genetic signatures relevant to the pathogenesis of the disease, the Pediatric Cancer Genome Project, and numerous other breakthroughs in research and diagnosis, as well as the exploration of rare and unknown diseases. He also co-founded a biotechnology company, Orion Genomics, applying genomics to human health and agriculture.

Cancer seems to be where many applications are now.

Why is that?

Cancer has been the low-hanging fruit for a couple of reasons. The first is that every cancer patient is essentially their own built-in control experiment. Starting with their biopsy sample, we extract DNA from tumor cells. We also extract some DNA from their normal body cells, maybe from blood. Then we sequence and compare both tumor and normal genomes. You look for the differences – mutations – that occurred in the tumor genome. And boom, maybe you've found the tumor's Achilles' heel. This has become relatively straightforward. The other thing is that, you know, it's cancer. If the standard of

"I THINK
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SYSTEM."

care treatments haven't worked for a patient and they are likely to have a very poor outcome, it often makes sense to pull out all the stops and see what you can come up with to treat them. So we have seen a lot of discovery and applications in cancer, and work continues on using this information to get better and better in decision making on treatment.

What's next in drug development based on genomic information?

When we first started sequencing cancer patients, I naively thought we were going to find mutations in certain cancer-causing genes, many of which would be new targets for drug development. Then we would wait 10 or 15 years for new drugs to be developed, brought through clinical trials, and regulatory approvals before patients received the drugs. And this is clearly happening, which is terrific. What I didn't realize at the time is that discoveries in cancer genomics would also teach us how to better use drugs that were already approved and simply in need of finding the right patients. That was and continues to be a big role for genomics. For example, when Iressa was first tested, it wasn't very effective for most lung cancer patients. But a fraction of those patients experienced an amazing response - their tumors virtually melted away. About this time, we sequenced several patients who happened to be enrolled in a clinical trial for Iressa. In nearly every patient who responded to the treatment, we found an EGFR mutation. So the answer was in their genomes - if you're a patient with that particular mutation, this is the drug for you. That was eye-opening. People started thinking about how we might be able to use the mutational profile of cancer genomes to better treat patients.

And now people are looking for genetic mutations across all kinds of cancer? Yes. And a big lesson of cancer genomics studies is that it doesn't matter so much what organ in the body a tumor arises from but what its genetic profile is. For example, we had an adult acute leukemia patient who had been through a bone marrow transplant, had two relapses and was in pretty bad shape, so we sequenced his genome. We found a mutation in a gene called FLT3, for which there was a drug that probably was a good candidate for him to try. Unfortunately, the drug was only approved for use in kidney cancer. His insurance company wouldn't pay for treatment, and the manufacturer wouldn't give him the

drug on compassionate use. Friends collected donations, over \$10,000, so he could have treatment. His cancer quickly went into remission, and it's been almost six years now that the patient has been cancer-free. So a powerful application that genome sequencing brings to the table is knowing how to better use drugs we currently have, and that will continue to expand.

How does a doctor use sequencing data? What does the doctor need to help a patient? Interpretation is the key. Most physicians are not going to know what to do with a result where you say, 'Hey, your cancer patient has a P53 mutation, but no mutation in RAS.' There are physicians who do know what to do when they hear something like that, but what most would prefer to hear is, 'Your patient has an EGFR mutation, and there are studies that show Drug X and Drug Y are good candidates for treating patients with those types of mutations. Also, the patient did not have a RAS mutation, so there's not any sort of contraindication to treating with an EGFR inhibitor.' In other words, most of them want to get a genomics report that's similar to what they get in a histopathology report – the findings, what they mean based on the literature, and a recommendation on how to turn this finding into treatment. Faster and better interpretation is an area where we really need to focus.

What's next in healthcare applications of sequencing?

Many diseases have genetic influences, either inherited or developed during life. There are as many potential applications as we have disorders. What we've started doing at Nationwide Children's is sequencing kids who have some sort of unexplained condition or disease, because these are difficult to treat without a better understanding. If you can find a potential causative variant in a gene, or multiple variants, you begin to take away the unexplained, and you may be able to treat that condition or at least provide helpful counseling to the family.

You have contributed to many milestones. Do you have a philosophy about what enables us to achieve breakthroughs? I'm not sure I can put my finger on it. I've been fortunate because I've been in the right place, the right situation, a bunch of times and that's worked out really well. Now, I do feel I had a prepared mind and, as Pasteur said, 'Fortune favors a prepared mind.' I was fortunate to meet the right people on several occasions – Bruce Roe who had just spent his sabbatical in Fred Sanger's lab and brought back those sequencing methods, Lee Hood at Caltech who developed so many new technologies, Jim Watson and others. You have to be in the right place at the right time, but you also need to have some vision and a pretty good idea of how to take the first steps. That combination leads to breakthroughs.

What about funding for research? Are we about where we should be?

We're not anywhere near where we should be. Right now we're in a terrifying situation in the United States with regard to the level of federal research funding, and we haven't been where we need to be for years. There was a period during the Clinton years in which a bipartisan decision was made to double the NIH [National Institutes of Health] budget. And that allowed an explosion of research, including much of the work in cancer genomics that has taken us so far down the road to better treatments. The reason we completed the Human Genome Project in

# "FASTER AND BETTER INTERPRETATION IS AN AREA WHERE WE REALLY NEED TO FOCUS."

the 2000s and applied genomic technologies to many diseases was because of the research budget that funded so much fundamental work. That budget has declined in recent years, and as a result, discoveries have started to fall off now.

There is a lot of amazing stuff we can do – so much that will translate into better outcomes for patients. To not be doing the kind of research we could be doing, and making discoveries for patients, it's just wrong.

And as sequencing for clinical diagnosis expands, is funding available?

Right now it's difficult to get insurance companies to reimburse for sequencing-based assays. Test costs are relatively high – though not as expensive as an MRI, for example – and insurance companies have a lot of competing costs. I would argue that if you sequence the genome of a leukemia patient, for example, the cost of sequencing pales in comparison to the cost of a bone marrow transplant, hospitalization, and potential lifelong treatment to manage immune response. If you had sequenced that patient, you may have found that they likely would have responded to a targeted therapy, and that a costly and dangerous transplant was not really indicated. We need to develop a better understanding of the value of testing relative to treatment so that insurers might realize the benefits of genome-based testing.

In your career in genomics, is there a single most gratifying project you worked on? I feel like our original work on AML, acute myeloid leukemia, was particularly important because it showed very clearly how genomics represented a powerful new approach to understanding the biology of a deadly disease. That work started to make a difference in how everyone looked at the application of genomics to cancer. So that's pretty satisfying. And then being able to move a lot of that work into the clinic. These days, the most exciting thing for me is not just to publish another paper or get a grant but to be able to say, 'Hey, here's another story about a patient whose genome we sequenced, and they're alive now and probably wouldn't have been if we hadn't been able to do that.' That's a gamechanger. It's hard to not feel fulfilled.



www.nationwidechildrens.org/ genomics-program





"We are the gatekeepers of the company. We make sure everything is correct and legal. If a new policy is launched in China or in Asia, first, we start to understand the key points, what we need to do and how we can follow that guideline, and then we communicate internally within the team and make sure everyone is on the same page. We also educate the sales team and the other departments so they can understand the new policy and requirements. If we find anything is wrong, then we contact the people and discuss it with them to make them understand the guidelines. But integrity is about more than just rules. I feel that integrity means something is whole, not broken, and it is strong, not weak. I try to carry that feeling to my team. We want that strength at QIAGEN itself, and we want it for our customers."

#### TRACY TANG

holds degrees in finance and business administration.

She joined QIAGEN in 2007.

Associate Director, Commercial

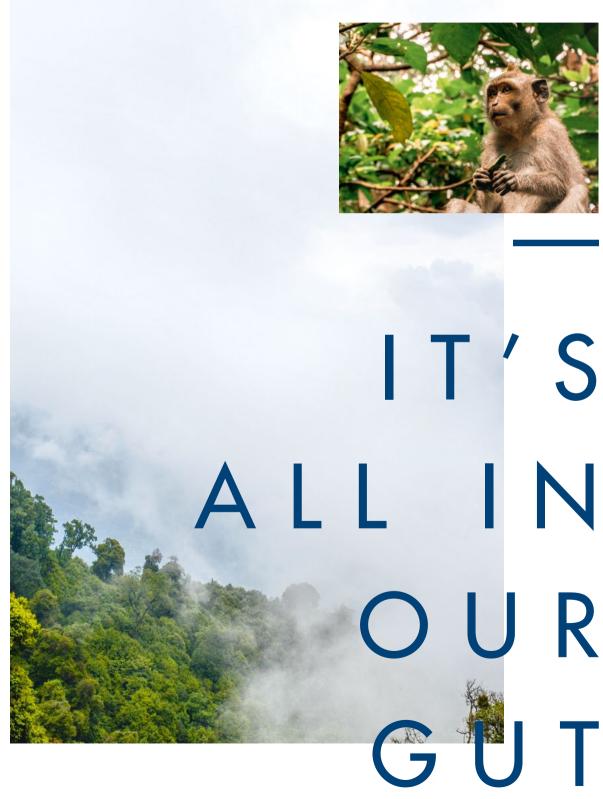
Operation Controlling, Shanghai City, China



>490

employees in various global functions including finance, legal, IT, procurement, communications and human resources keep an eye on the smooth and reliable flow of QIAGEN's business processes.

## BEHAVIOR





From wildlife researcher to computational biologist: Dr. Mike Montague



\_\_ Does the way we behave depend in part on the specific community of microbes living within each of us? Dr. Michael Montague studies the microbiome of a free-ranging population of primates to understand how it shapes their social interactions and vice versa.

> Good news was followed by a disaster. Just a few days after Michael Montague heard that he won the 2017 QIAGEN Microbiome Award, Hurricane Maria devastated much of Puerto Rico. The hurricane also swept over a small research island called Cayo Santiago, where scientists have been observing hundreds of rhesus macaque monkeys for decades. The island was the precise spot where Dr. Montague had planned to realize his project.

What can you tell us about the current situation on Cayo Island?

Fortunately, all of the monkeys survived the storm and its aftermath. But our entire research infrastructure was erased by the hurricane, all facilities were destroyed and are in need of rebuilding. We have begun raising funds for the long rebuilding process, but it will take several months until my research will be possible again.

Why is this spot special? | The ancestors of these monkeys were originally moved to the island from India in 1938, making it one of the oldest primate research centers in the world. For eight decades and over nine generations, the births, deaths, and group dynamics have all been charted. This makes it an incredibly unique resource for understanding how they think, choose friends, choose mates, and the genetic underpinnings of their complex social behaviors.

#### But how are monkeys connected to your field of research, the microbiome?

We want to test whether the microbiome and behavior influence each other. Monkeys live in large social groups of 80 to 300 animals. A number of social units, characterized by stable female family groups, exist in these groups. Male monkeys often move within and between different social groups. Our research team was already able to show that monkeys from different social groups show changes in their microbiomes.

#### Is the microbiome linked to social behavior?

That is what studies on wild chimpanzees and baboons have shown. In humans, microbiome variation is also linked to health issues, such as obesity and autoimmune disorders. So different questions arise, including how might animals modify their behavior to maintain a healthy and diverse set of microbes. It's likely that beneficial microbes provide animal hosts with the immunity and metabolism to forage and find mates, strengthen their social interactions with their preferred group mates, and – most importantly – avoid predators or other threats.

#### So what will your QIAGEN-supported project look like?

Our proposal specifically examines how varying degrees of social interaction impact the gut microbiome in rhesus monkeys, while also exploring how the diversity of gut microbes influences levels of peripheral and central serotonin. Some species of gut bacteria can directly metabolize tryptophan, a crucial precursor used in the manufacture of serotonin. Competition for tryptophan is therefore likely to impact host serotonin availability.

#### Why do you look at serotonin?

Serotonin is a key neurotransmitter influencing our digestive tract, cardiovascular system and our brain. It is known to play a role in modulating mood, appetite, sleep, cognition, arousal or pain – thus, it also has an important effect on behavioral patterns.

#### DR. MICHAEL MONTAGUE

of the University of Pennsylvania is the winner of the 2017 Microbiome Award. As an undergraduate at Boston College, he majored in biology and excelled in genetics and molecular biology. While contributing to research projects in wildlife biology, he became fascinated with topics in evolutionary biology and animal behavior. He obtained a doctoral degree in primatology and genetics from New York University, followed by a three-year postdoctoral position in genomics and computational biology at the McDonnell Genome Institute at Washington University's School of Medicine.





## "THE COEVOLUTION OF HOSTS AND THEIR MICROBIOME REPRESENTS A COMPLEX AND INTEGRATED ARRANGEMENT."

#### Can you tell how your project will unfold?

We will first measure female grooming behavior, followed by shotgun sequencing of gut microbiomes from fecal samples and serotonin collection from various bodily fluids. We expect socially integrated females who interact more frequently in grooming to possess more diverse gut microbiomes and different levels of serotonin. Resulting data will enable us to clarify how the gut microbiome affects serotonin synthesis and the potential effects of serotonin and gut microbial composition on social behavior.

#### Do you see any implications of your research for humans?

We can use our findings in monkeys as a guidepost for understanding the biology of both normal and atypical human behavior. How exactly do our deeper and more numerous connections makes us healthier, happier, and live longer? Such knowledge may help design new treatments for human disorders. There's, for instance, increasing evidence that changes in tryptophan or serotonin levels in the gut may be important for understanding disorders of the central nervous system.

In your research you combine more traditional field research with modern molecular technologies. What kind of biologist are you? As a student I carried out field research. But today I consider myself a computational biologist, so much of my time is spent working with and analyzing genomic data from our primate research population. We've recently generated some gene expression data from different types of tissues, including blood, and of course our team is heavily invested in developing more results from the data we generated from skin and fecal microbiotas.

#### Do you use QIAGEN technology doing your work?

I made use of QIAGEN extraction kits throughout my graduate training. They were easy to use and produced quality template DNA from low-quality fecal samples collected in the field. Our current work on skin and fecal microbiomes makes use of the DNeasy Power Soil Kits.

#### What is your ambition with this research?

The coevolution of hosts and their microbiome represents a complex and integrated arrangement. If we can illustrate a comprehensive picture of microbiome diversity within the context of a population's social structure, then we might gain a better appreciation of being social as an evolutionary mechanism. I anticipate testing whether and how varying degrees of social integration impacts the microbiome and serotonin levels, since this represents a critical step in our understanding of the gut-brain axis.

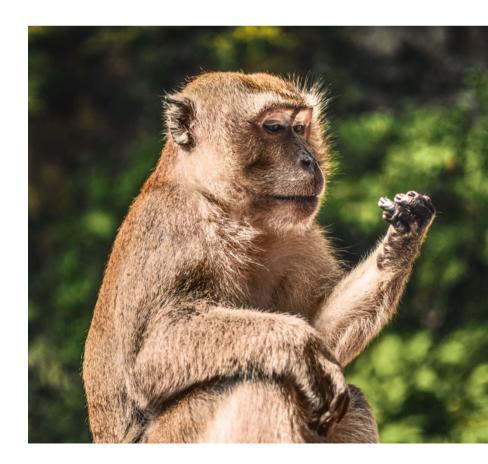
Do you find it more fascinating or more frightening that our behavior is possibly shaped by countless microorganisms in and around us? I'm fascinated by this idea. This is really about the big question of how our brain processes information to elicit certain behaviors, specifically spontaneous behaviors such as laughing. How might our moods and reactions be shaped in part from viruses and bacteria? If you add the question about how different behaviors evolved in the first place, and ponder the microbiome's role in all of this, then these are extremely exciting questions. Individuals and the microbiome influence each other mutually; we are part of one ecosystem.

#### THE AWARD

The Microbiome Awards provides young, extraordinary scientists with funding and recognition to carry out scientific work in the field of Microbiome research. QIAGEN, the main sponsor of the award, is generously donating a prize package for the 2018 Microbiome Awards. This year's awards will be open to scientists who received their PhD in 2008 or later and will also include a new category for PhD students. Applications will be accepted beginning in May 2018.



http://bit.ly/MichaelMontague http://bit.ly/MicrobiomeAwards2018



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As of February 2018, QIAGEN molecular diagnostics products included 18 FDA (PMA approved or 510k cleared) products, 16 clinical sample concentrator products (13 kits and 3 instruments), 62 EU CE IVD assays, 16 EU CE IVD sample preparation products, 17 EU CE IVD instruments for sample purification or detection, 29 China CFDA IVD assays/sample preparation and 13 China CFDA IVD instruments.

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This document contains detailed financial information about OIAGEN prepared under generally accepted accounting standards in the U.S. (U.S. GAAP) and included in our Form 20-F annual report filed with the U.S. Securities and Exchange Commission. OIAGEN also publishes an Annual Report under IFRS accounting standards, which is available on our website at www.QIAGEN.com.

#### QIAGEN AT A GLANCE

#### **Product Categories**

13%

#### Instruments

are used with consumables, enabling customers to automate processes from the preparation of clinical samples to the delivery of valuable results. Percentage share of 2017 net sales

87%



#### Consumables and related products

are specialized kits that contain all necessary materials to support the use of sample and/or assay technologies as well as bioinformatics solutions for analysis, interpretation and reporting of biological data.

#### **Customer Classes**



#### **Molecular Diagnostics**

Physicians, hospitals and healthcare providers use QIAGEN technologies to save lives and fight disease. Our products support disease prevention such as screening women for risk of cervical cancer, profiling patients to pinpoint many diseases, personalized healthcare to guide treatment decisions, and point-of-need testing to provide onsite diagnosis.



10%

#### **Applied Testing**

Professionals in fields such as human identification and forensics, food testing and veterinary medicine use QIAGEN technologies in commercial applications beyond human healthcare. Our products help to solve crimes, secure food supplies and detect potentially devastating livestock diseases.



18%

#### Pharma

Scientists in the pharmaceutical and biotechnology industries look to QIAGEN to advance gene-based drug discovery and development, supporting the creation of new medical breakthroughs.





#### Academia

Researchers at life science laboratories around the world depend on QIAGEN to advance our understanding of the molecular basis of life. Customers include universities and research institutes.

