INSIGHTS

THE QIAGEN MAGAZINE 2019

Sample to Insight

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 we don't even realize.

Samples Genomic Data = >1.5B DVDs annually

The challenge

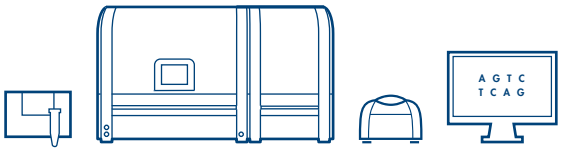
Gaining access to valuable molecular insights – and understanding their impact – remains elusive and challenging.

Costly Lengthy Unreliable

THAT'S WHY QIAGEN EXISTS

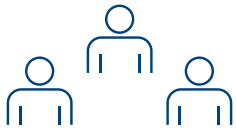
Every day we help more than 500,000 customers gain the valuable molecular insights they need

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.



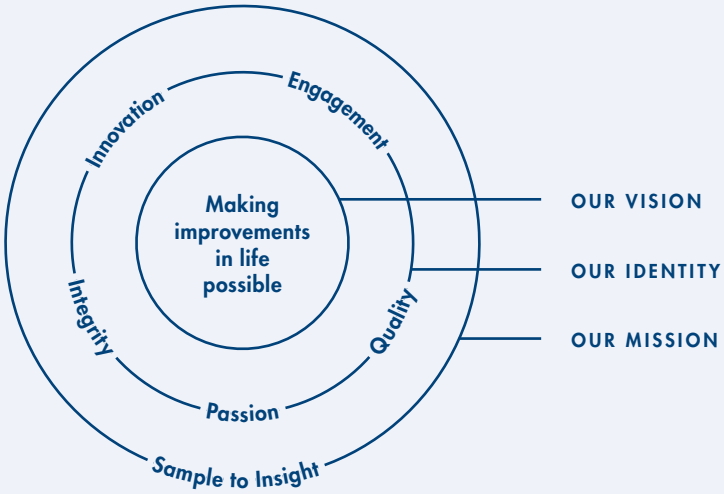
Bring together 5,000 passionate QIAGENers who are driven by the impact of their work and to excel in helping customers exceed their own expectations.

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

MAKING IMPROVEMENTS IN LIFE POSSIBLE

SAMPLE TO INSIGHT

Sample to Insight is our strategic framework that puts the needs and challenges of our customers front and center. We want to identify key challenges holding customers back and to deliver solutions so they can achieve greater success, ultimately helping them exceed their own expectations and gain the insights critical for their work.



OUR VISION

At the core of a great company is the ambition to make a difference. It answers the question why a company exists. At QIAGEN, we have a truly exciting vision, and the future we seek is meaningful – making improvements in life possible.

OUR MISSION

Our mission defines our purpose, what we do and how we make an impact. As the innovative market and technology leader, QIAGEN creates Sample to Insight technologies that enable access to valuable molecular insights from any biological sample. Our mission is to make improvements in life possible by enabling our customers to achieve outstanding success and breakthroughs in life sciences, applied testing, pharma and molecular diagnostics.

Our commitment to the markets, customers and patients we serve drives our innovation and leadership in all areas where our Sample to Insight technologies are required. The exceptional talent, skill and passion of our employees are key to QIAGEN's excellence, success and value.

OUR IDENTITY

Our 3i framework expresses our culture, leadership principles and how we act at QIAGEN. It anchors our aspirations of focus, accountability and entrepreneurial decision-making.

Identity
Our culture is shaped by our values

Passion / Quality
Integrity / Engagement
Innovation

Inspire
Our leadership style transmits our values and inspires our employees

Influence / Motivate
Stimulate / Develop

Impact
Our value-based actions make the difference

Entrepreneurial decision-making / Focus /Accountability

OUR PEOPLE

The greatest strength of QIAGEN is our people. Their diversity, energy, expertise and creativity are critical to our success.

> 5,000
employees worldwide

> 70
nationalities

34
countries with direct QIAGEN operations

OUR STRATEGY

Our strategy is to address the rapidly changing needs of our customers, providing solutions that enable them to gain valuable molecular insights from any biological sample. As we implement our strategy, we focus our teams on five priorities to create value for our stakeholders.

Accelerate growth

We are focusing on key franchises driving growth across the customers we serve worldwide.

Enhance growth with acquisitions and integration

We are complementing internal R&D with new business opportunities that strengthen our Sample to Insight portfolio.

Deliver efficiency and effectiveness

We are rethinking how we work, embracing agile teams, digitization trends and building better productivity.

Increase value of QIAGEN as employer of choice

We are building a culture in which our employees can fully apply their talent and energy and share in the rewards.

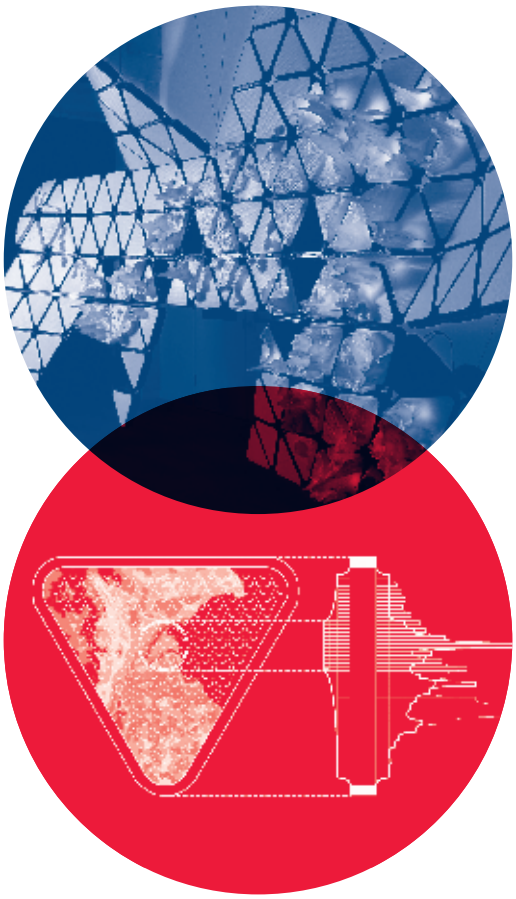
Enhance customer experience

We are determined to exceed the expectations of our customers in helping them gain the insights they are seeking.

INTO DEEP WATERS

Every organism leaves its mark on this planet, one way or another. As different species interact with the environment, they expel DNA as they shed skin fragments, larvae, feces, or other bodily traces, which accumulate in their surroundings. Scientists collect this environmental DNA (eDNA) to better understand biodiversity in the past, present, and future – and use this information to help fuel conservation efforts around the globe.

THE ART OF DNA



There is beauty in biology – and in the exploration of life at every level. Today, from nano-architecture to induced pluripotent stem cells, scientists and artists use biology as a medium to create art and bring innovation to light. Just look at the Bio City Map of the artist Mitchell Joachim from Terreform ONE in New York. It displays population density of 25 mega-cities as a parametric graph with a background of living biosynthetic transgenic matter that consists of billions of bacterial cells. Two different forms of fluorescent transgenic *E. coli* represent existing demographic conditions (glowing green) and future census projections (glowing red). The genetic modifications were carried out at Genspace, which is based in Brooklyn, New York, and is the world's first community-based biotech laboratory, and at Terreform ONE, an NGO for philanthropic architecture and urban and ecological design.

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WHO AM I– AND HOW MANY OF ME ARE THERE?

Even though every human life begins with a single cell, recent research reveals that every person has not one but multiple genetic identities. Even the brain knows more than one version of itself, and every tissue consists of several cell lines with a clearly distinctive genetic profile. This phenomenon is driven by numerous mutations and division errors, which accumulate in the cells and create diversity – and in the fight for a fixed place in the body, are sorted out along with the cells. Researchers say the different cell groups form a mosaic in the body, which is why the phenomenon is called mosaicism.

THE SKY IS THE LIMIT

On Earth, various molecules band together in liquids, assembling into uniform and repeating patterns. But will these molecules behave in the same manner, crystalizing into predictable forms, when placed into a microgravity environment? To test this hypothesis, the National Aeronautics and Space Administration (NASA) launched a new project called Real Time Protein Crystal Growth (RTPCG), in which astronaut researchers will make use of QIAGEN's EasyXtal plate to discover how organic chemistry may differ in space.

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THE UNKNOWN UNIVERSE BENEATH OUR FEET

The last white spot on this planet? Just look for it ten centimeters beneath your feet. The soil is a universe of its own: a place where above-ground principles are not in force and where most of the planet's inhabitants live. The number of organisms found in a handful of soil far exceeds the number of humans who have ever lived. There are microbes, fungus and bizarre creatures; the springtail, for instance, has eight eyes and is blind. The biological activities of species like these and their interactions shape our world above, creating a viable surface for our existence. For some, soil is the biggest organism on this planet. Still, most of this world remains unknown. Modern technologies for isolation of microbial genomic DNA, like QIAGEN's DNeasy PowerSoil Kit, have significantly helped to decode the terra incognita beneath the surface.

MOLECULAR COMPUTING

Pioneering researchers led by Dr. Lulu Qian at the California Institute of Technology (Caltech) in Pasadena, California, have created an artificial neural network consisting of DNA instead of computer hardware and software. This type of machine-learning method is based on synthetic biochemical circuits to perform information processing at the molecular level. One day, that could lead to a DNA-based computer that is small enough to run inside a single cell. In 2018 Dr. Qian demonstrated such a setup that can correctly identify the handwritten numbers 1–9 to a 10×10-pixel grid. Even when 30 of the 100 bits of a given pattern are flipped – analogous to the variation in handwritten characters – their network can "remember" the pattern correctly and recognize the digit. This suggests that molecular computation circuits can classify highly complex and noisy information based on something akin to memory.

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*QIAstat-Dx will be available in 2019. Product is currently marketed under the name DiagCORE and not available in all countries.

MOVING INTO A NEW PHASE

CEO Peer M. Schatz discusses the driving factors behind QIAGEN's successes in 2018 and the strategy for strengthening its leadership position and Sample to Insight framework.

After a year of solid growth in 2018, what's next for QIAGEN?

PEER SCHATZ I would like to first thank all of our associates worldwide for the very strong performance in 2018, a year in which we made further progress in transforming our portfolio. We have now assembled what I believe is a most disruptive and dynamic portfolio of Sample to Insight solutions for molecular testing. Based on our efforts, QIAGEN is positioned better than ever before to help our customers gain valuable insights from any biological sample. We are moving into a new phase with a commitment to delivering on the promise of this portfolio.

What have you done to create this portfolio and what are your differentiated areas?

We have assembled this portfolio through our own internal innovation and development as well as through targeted acquisitions focused on some of the most exciting areas of molecular testing. For example, our QuantiFERON-TB test has strengthened its position as the modern gold standard for detection of the latent form of tuberculosis, which remains a stubborn global health issue. We also have an outstanding portfolio of solutions for use in next-generation sequencing (NGS), an exciting technology that is helping customers gain deep and rich insights into DNA and RNA – the building blocks of life. We are also launching new automation systems in large and growing markets for molecular testing. These new integrated platforms, QIAstat-Dx and NeuMoDx, are highly complementary additions to our modular QIAsymphony flagship automation system, which reached a milestone with over 2,300 cumulative placements at the end of 2018.

As the pace of genomic discoveries accelerates, how will QIAGEN remain a global leader?

In the 21st century, discoveries emerge at the cutting edge of life science research and move forward very quickly to become clinical applications, improving outcomes and the lives of people on a daily basis. Our strategy is to engage with our more than 500,000 customers worldwide. The 2018 Nobel Prize for Physiology or Medicine is an example: Two scientists, in California and Japan, were honored for making discoveries about the immune system that have led to a new way to fight cancer called immuno-oncology, where targeted therapies are used to train the body's immune system to fight cancer cells. QIAGEN solutions helped these Nobel laureates as well the scientific communities to achieve their research breakthroughs that are changing our daily lives, and today we are developing companion diagnostics for leading pharmaceutical companies to help guide clinical decision-making for immuno-oncology drugs. QIAGEN has a differentiated strategy to support our customers across this continuum. And this is how we create value for them and our stakeholders.

> **"WE HAVE A MOST DISRUPTIVE AND DYNAMIC PORTFOLIO."**
>
> **PEER M. SCHATZ**

So how does Sample to Insight help you as a strategic framework?

Sample to Insight means focusing on what customers want to achieve with molecular testing: The focus is not on technologies, but on the valuable insights our customers are seeking. We want to assemble solutions in our portfolio with the goal of exceeding expectations of our customers for what QIAGEN can do to support them – whether it be a breakthrough sample technology such as liquid biopsy, or a complete workflow such as the GeneReader NGS System.

How has QIAGEN evolved over the years?

QIAGEN has long-standing relationships and an exceptional reputation in academia and industry for highest-quality products and superior customer service. We have always sought to understand the needs of scientists and to provide solutions to address their constantly expanding range of molecular testing needs. In the early days of QIAGEN, the need was reliable and consistent ways to extract and purify DNA and RNA from biological samples, which remains a crucial first step for molecular testing. Shortly thereafter, we

expanded to offer assay technologies like PCR and NGS, which analyze and interrogate genomic samples for the insights sought by our customers. We have also offered generations of automation systems to make molecular testing faster, better and easier for our customers. We placed significant priority on creating tests to run on these systems, and today QIAGEN offers a wide range of molecular assays for diagnostics and research use. In recent years, we have created an industry leadership position in bioinformatics, an increasingly critical step for customers to analyze and interpret the vast volumes of genomic data being created through NGS. In sum, QIAGEN has a unique strategic agility that we have developed as our industry has expanded, above all working in close collaboration with our customers. This is how we deliver Sample to Insight.

Could you give some examples of how innovation occurs in the Life Sciences?

Innovation applies to completely new breakthrough solutions, as well as improvements to our current portfolio. One of the rapidly expanding areas in Life Sciences research is RNA sequencing. A major impediment is that most types of RNA contained in cells are not relevant, so preparing RNA for sequencing can be slow and cumbersome. QIAGEN solved that problem in 2018 with a completely new breakthrough called QIAseq FastSelect RNA Removal Kit, which enables customers to target and remove RNA types in one step that are not relevant to their work. This dramatically reduces the processing time from over two hours to about 20 minutes. An example of enhancing our current portfolio is the new generation of our QIAcube instrument for sample processing, which we launched in early 2019 to deliver a new level of digitization and ease of use. This builds on the 8,000 placements of the first-generation system that is a mainstay for many research labs worldwide.

Moving to clinical healthcare, where does QIAGEN stand in Molecular Diagnostics?

Our focus in Molecular Diagnostics is on offering solutions that can make a difference for labs in terms of helping them improve outcomes for patients in the most effective and efficient way possible. QIAGEN is one of the largest players in molecular diagnostics, and focused on very attractive opportunities in Immune Response with our QuantiFERON-TB test for latent TB, a wide range of Infectious Diseases with our expanding range of automation systems (QIAsymphony, QIAstat-Dx and NeuMoDx) combined with a deep menu of tests, and Precision Medicine with our portfolio of PCR and NGS assays to support advances in guiding treatment decisions for patients, especially those with cancer. Clinical products and solutions often develop from breakthroughs developed by our customers in Academia and Pharma, a confirmation of the strategy to support customers across this continuum.

QIAGEN's top-selling product is the QuantiFERON-TB test for latent tuberculosis detection, which is part of the Immune Response franchise. Where do you see QuantiFERON-TB in its product life cycle?

QuantiFERON-TB is the gold-standard blood test for latent tuberculosis (TB) infection, being used by customers worldwide to replace the use of the 120-year-old tuberculin skin test. We are still in the early stages of converting the global market for latent TB testing, which is estimated at more than 70 million tests annually. We are now in the fourth generation, with QuantiFERON-TB Gold Plus (QFT-Plus) approved in more than 75 countries globally. QFT-Plus grew at a strong 20% annual pace in 2018 as awareness of the benefits grows and new guidelines are calling for greater TB control, and we expect a solid double-digit growth pace in the future. We are enhancing the automation options for QFT-Plus through partnerships with DiaSorin, Hamilton and Tecan to enhance the efficiency of testing, also for national TB programs. We are also developing QuantiFERON-TB Access and preparing for launch in 2020 to make blood-based latent TB detection accessible to low-resource regions with a high disease burden. Given that the overall market for latent TB testing is only about 15% converted to the modern blood-based test, we see significant growth potential and are on track to achieve our target for $300 million in sales in 2020.

"SAMPLE TO INSIGHT MEANS TO FOCUS ON CUSTOMER NEEDS."

In Infectious Diseases, you have launched QIAstat-Dx for syndromic testing and NeuMoDx with two new integrated testing platforms. What is their potential?

Infectious disease testing represents a market opportunity of nearly $4 billion, and the QIAstat-Dx and NeuMoDx solutions are opening up significant new opportunities. In April 2018, we acquired and launched QIAstat-Dx, a unique and differentiated system that represents a new generation for syndromic testing, which is helpful for diagnosing patients with symptoms against a range of pathogens. This is an $800 million annual market opportunity growing at a double-digit pace. In September 2018, we entered the $2.7 billion market for fully integrated PCR analysis with the NeuMoDx 288 and 96 platforms. The first step in our partnership is a European distribution agreement, and we have the option to fully acquire NeuMoDx by mid-2020. NeuMoDx delivers dramatic workflow advantages for high-throughput and mid-throughput testing, with the ability to automate practically any PCR test custom-

ers need to process. With these disruptive Sample to Insight systems, QIAGEN can now engage nearly the entire global market for molecular diagnostics.

What are your expectations for QIAstat-Dx?

QIAstat-Dx is a one-step, fully integrated system with important advantages for near-patient analysis of common syndromes in Infectious Diseases, plus potential for expansion into oncology and other conditions. With less than one minute of hands-on time and results in about an hour, QIAstat-Dx can differentiate the cause of hard-to-diagnose syndromes. Cost-efficient, single-use cartridges powered by QIAGEN chemistries provide best-in-class sample preparation and processing with all reagents on board. QIAstat-Dx is rapidly gaining acceptance in Europe after launching in 2018 with panels for respiratory and gastrointestinal infections, and we expect to launch in the United States in 2019. We have a deep pipeline of tests in development, in particular a panel for meningitis.

Why do you consider the NeuMoDx systems – the 288 and 96 – disruptive?

The NeuMoDx systems introduce modern Sample to Insight solutions into mid- to higher-throughput molecular diagnostics, which are primarily used in centralized labs. Existing automation is dominated by older technologies for liquid handling, with time-consuming, inflexible and expensive workflows. NeuMoDx provides automation of the complete workflow through use of advanced microfluidics and other technologies that dramatically simplify the workflow and speed up analysis. Some tests can be processed in as little as 40 minutes, and this compares to over three hours on other platforms. The feedback from our launch in Europe has been exceptionally good. We look forward to growing NeuMoDx as more labs embrace this modern solution for integrated PCR testing.

These new automation systems are a big addition to your flagship QIAsymphony automation system. What is the role of QIAsymphony in QIAGEN's future?

QIAsymphony is a world-class solution and is expected to have a great future. The flexible modular approach of QIAsymphony has been transformative for laboratories in many molecular testing applications. Some labs prefer the modular PCR format of QIAsymphony, while others will want the integrated approach of NeuMoDx. In 2018 we surpassed 2,300 cumulative QIAsymphony placements around the world, and we set a new target to reach over 2,500 by the end of 2019. One of the growth engines for QIAsymphony has been the use of its automated sample processing to support labs in handling the rapid growth in processing samples for a range of downstream applications, including PCR and NGS. In recent years, sample processing has represented by far the majority of placements, highlighting the limited overlap with the growth opportunities for NeuMoDx. As molecular testing continues to proliferate, QIAsymphony is a proven workhorse with a bright future.

"WE HAVE EVERYTHING IN PLACE TO ACHIEVE SUSTAINABLE GROWTH."

In Precision Medicine, formerly known as Personalized Healthcare, your efforts have shown rapid progress. What is the future for QIAGEN in this area?

The fast-growing use of genomic information to diagnose and guide treatment offers dynamic growth potential. QIAGEN is the worldwide leader in partnering with pharma and biotech companies to create companion diagnostics to determine the molecular profile of cancers. This molecular information can be used to stratify patients and decide what therapies would be most appropriate. It can also be used to supporting dosing and to monitor disease progression. Precision Medicine continued to grow in 2018 and is above $120 million of annual sales, with an expanding menu of companion diagnostics and more than 25 pharma partnerships. Our deep pipeline is expected to produce a stream of new product launches. Along with new biomarkers and gene panels, we are expanding our bioinformatics to enable new insights not even conceivable a few years ago. Precision Medicine has a long runway for growth in oncology and hematology, with future expansion into other disease areas.

As an emerging technology platform, what role does NGS play in QIAGEN's future?

We exceeded our goal for $140 million of NGS-related sales in 2018, about 10% of our sales, and set a new target for $190 million in 2019. Our strategy has two prongs: universal solutions addressing the full range of lab needs using any NGS platform, and our complete and fully integrated GeneReader NGS System for use in targeted gene panel sequencing in clinical research and selected forensics applications. Our universal products are used in nearly every NGS lab around the world, and we keep on innovating. Our RNA sequencing solutions, QIAseq gene panels, immuno-oncology tests and custom NGS assays are recognized as differentiated products that make QIAGEN a leader. Meanwhile, GeneReader is benefiting from placements and growing consumable sales. We launched new GeneRead QIAact gene panels in 2018 for breast cancers, myeloid malignancies and other tumors, as well as offering customers the opportunity to order custom panels. NGS is still in its early days, and we are becoming a bigger player in a segment that will become increasingly more important for our customers in the coming years.

As NGS technology becomes more prevalent, the amount of data being generated is exploding. What do you see as the role of bioinformatics in the QIAGEN portfolio?

The immense power and potential of NGS will be difficult to translate into improved outcomes for patients, along with greater efficiency in the healthcare system, without solutions that help derive insights from massive volumes of data being generated by NGS systems. We are convinced that future value creation and differentiation of NGS workflow solutions will be driven increasingly by content and applications, and less and less by sequencing hardware and chemistry reagents. This is why we have developed QIAGEN Clinical Insight (QCI) to support clinical decision-making, backed by the industry's deepest knowledge base of genomic insights. We are continually enhancing QCI, for example with our recent acquisition of N-of-One to integrate real-world evidence into the insights. Another example is the selection of our HGMD database by the United Kingdom's 100,000 Genomes Project and then NHS England to transform the understanding and diagnosis of hereditary diseases. QIAGEN bioinformatics deliver insights from any sequencing platform, but provide great value to our own solutions through seamless integration.

"OUR WHOLE MINDSET IS BUILT AROUND SERVING OUR CUSTOMERS."

How are you changing the way you work at QIAGEN?

Our whole mindset is built around serving customers and helping them exceed expectations for how our Sample to Insight portfolio can support them. We put customers at the focus of everything we do, from helping researchers get actionable insights to helping clinicians improve outcomes for patients. We track performance quantitatively and look at many aspects of customer interactions. Our Customer Experience Indicator in 2018 showed that our employees are performing at a very high level against expectations. We also met ambitious goals for innovation, measured through our QIAGEN Vitality Index. Digitization is changing the way we interact with customers and how we work – in 2018 more than 40% of sales came through digital channels, and our goal is 50% in 2020. Above all, we focus on the human factor – making QIAGEN the industry's best place to work – because people drive performance.

As a final topic, what does the future hold for QIAGEN?

Customers are giving us feedback that we have built a dynamic and disruptive portfolio. We have powerful, growing franchises in molecular testing, along the continuum from basic research to routine clinical care. We have all the resources in place to achieve ambitious targets for sustainable growth. Our focus now is on executing, making progress every day to deliver on these growth opportunities and make improvements in life possible. This is how we can continue to create tremendous value for QIAGEN customers, employees and stockholders.

CUTTING TIME

IMPROVING OUTCOMES

A pioneer in syndromic testing – the Bichat Claude-Bernard hospital in Paris.↑

A cotton swab with sample DNA is placed in a cartridge for the readout.→

Influenza, or a different respiratory infection? QIAstat-Dx – QIAGEN's new system for syndromic testing – helps doctors in emergency rooms save precious time and decide on the right treatment, isolation and management for their patient. A visit at the Bichat Claude-Bernard hospital in Paris – at the height of flu season.

Suddenly, there is a cry of "Sac de réanimation!" – a resuscitation bag is needed. There is a jumble of intensive care nurses and doctors in green scrubs, and emergency personnel wearing yellow. Running ahead of a hospital bed carrying an elderly man covered by plastic tubes, they shout for everyone else to make way.

It's early winter in Paris, and the Bichat Claude-Bernard hospital is gearing up for an influx of influenza patients. The hospital is a marriage of a squat building of red and yellow bricks to an imposing high-rise made up of a jumble of glass and steel boxes dating to the 1970s. Sitting just inside the boulevard périphérique, the beltway that separates Paris from its suburbs, it doesn't have much of a revolutionary air.

Here, though, a small revolution in the diagnosis of infectious diseases is taking place – that is what **Benoît Visseaux**, a virologist and self-proclaimed "lab guy," sees behind the hospital's QIAstat-Dx, QIAGEN's new system for multiplex syndromic testing. "It will help us to perform better," says Visseaux while he strides down hallways painted pale yellow, through doors that must be swiped open. Beneath the sign "salle de déchocage," double doors swing open, and behind three hospital beds shielded by fabric screens, a box the size of a small printer sits on a table.

H 1 N 1

Ease to use – Benoît Visseaux with Christophe Choquet, a colleague from the emergency unit, in front of the QIAstat-Dx. ↑

Readout within an hour

QIAstat-Dx, launched in Europe in the fourth quarter of 2018, represents the next generation in multiplex molecular diagnostic systems, based on real-time PCR technology that can process up to 48 targets. With novel Sample to Insight solutions powered by QIAGEN chemistries, it enables fast, cost-effective and flexible syndromic testing.

In the past, doctors only had incomplete information when starting treatments or isolating patients, as patients often enter the emergency room with a number of symptoms that don't allow for a clear diagnosis. Now, through syndromic testing, the QIAstat-Dx gives doctors, nurses and technicians a readout within an hour as to which respiratory or gastrointestinal pathogens ail the patient.

The machine is small enough to find a spot in a crowded emergency room without getting in the way, and its ease of use is such that it can be run by both nurses and technicians, even when the testing itself is complex and cutting edge.

"The emergency room is the point where such information is most useful," explains Dr. Visseaux, a thin man with a stubbly beard, wearing a white lab coat with at least seven pens in his breast pocket. The speed of the test allows doctors to make important decisions on the spot. "You have to deduce if the patient should be hospitalized or not," he says. "You have to protect other patients if the patient is infectious."

A mortal disease

Dr. Celestin Alexis Agbessi, a bearded physician in blue pants and a burgundy sweater, who stops to clean his glasses every so often, says: "QIAstat-Dx is a major step for flu patients." The reason why not everyone will be tested is that the mortality rate of flu increases with age and history of disease. "That's why we have to be selective. At this point, we only use QIAstat-Dx for patients with HIV, cancer, lymphoma, diabetes or those whose excess weight complicates their diseases."

Beep, beep, beep. The commotion dies down, and inside the shock room,

Open your mouth, please – Dr. Agbessi gets a sample with a swap from a patient. ↑

"YOU CAN GIVE THE PATIENT THE RIGHT TREATMENT IN ONE HOUR."

DR. CELESTIN ALEXIS AGBESSI

where a nurse in green works at a computer, the elderly patient who was brought in moments ago already has a glucose drip inserted into his arm and is being tested for respiratory pathogens. A technician dons a pair of gloves and pulls a swab from a glass vial to gather material from inside the patient's nose. The swab is then placed into a QIAstat-Dx cartridge. The technician snaps off the end of the swab and closes the cartridge in one deft movement. After scanning the bar code of the cartridge, it's gently loaded into the QIAstat-Dx machine. The short wait of about an hour leaves doctors enough time to administer the right drugs, choose a correct antibiotic, and decide whether to isolate the patient or even discharge one whose test doesn't show a serious infection.

"If you have a result, you know which kind of virus is the problem – influenza A, coronavirus or RSV – and you can give the patient the right treatment in one hour," explains Agbessi. The machine, with its two panels, can identify 21 viruses and bacteria in its respiratory panel, and 24 pathogens and parasites in its gastrointestinal panel. Through amplification curves, it can also determine co-infections and their relative strength. "Before, a patient might have the flu, but you might treat him unnecessarily," notes Agbessi, pointing out that all treatments are costly and have side effects. "This test is what allows us to decide what is right."

Tube to the lab

As a cold wind snaps the tricolor French flag flying high above the hospital, and scatters icy rain on the pavement, Benoît Visseaux exits the building, heading past the ambulance bay and the hospital's entrance to the laboratory that initially housed the tests, a placement that slowed results.

L 6 3

Just a few minutes later, Dr. Agbessi starts the QIAstat-Dx run.↑

QIASTAT-DX IS AN EASY-TO-USE SOLUTION FOR FAST AND RELIABLE DIAGNOSIS OF COMPLEX SYNDROMES.

Market outlook

Around 1.1 million tests per year in Europe and 1.5 million in the United States are projected for QIAGEN´s respiratory panel.

The broader pipeline of assays and applications for QIAstat-Dx spans infectious diseases, oncology and companion diagnostics, quantitative analysis and immunoassay testing.

The additional capability to process immunoassays creates unmatched target and application versatility, as well as disease management options.

"The first point is, you have to send the tube to the lab," he says, describing how it was done in the past. The hospital runs a pneumatic system, which can speed up the process, but first it goes to a central room, upon which everything is dispatched into all the labs. "This system takes a lot of time, a least one hour, and that's when everything is going very, very well," says Visseaux. In his experience, in real life, the sample won't arrive in the lab for at least two hours. "Most of the time it's even worse, especially at night, or on the weekend."

QIAstat-Dx provides results much faster, or like Dr. Visseaux says: "We get the results already with the patient at the entrance of the hospital." But there's more to it than that. It has also led to some unexpected insights, says Dr. Visseaux, adding that it used to be that the respiratory syncytial virus, or RSV, was thought to be the cause of severe respiratory illness only in children. Such testing has now shown that it lies at the root of many severe infections in adults as well. "Now that we are testing almost all respiratory viruses at once, we have a lot of new questions."

Agbessi is convinced that the little box not only reduces the time patients must stay in the hospital or even be isolated, and the amount of drugs prescribed, but that it has also changed the practice of medicine at Bichat Claude-Bernard Hospital. "It changed our perception, our prescription habits, and it will change the way we work in the future." What Alexis Agbessi is also sure about is that if you change prescription habits and how you think about the patient, you save money, you see fewer side effects, you use less antibiotics and you save time. "In the end, we gain money for both the community and the patients. That is really a big step forward."

CLEAR YET DANGER

Tuberculosis claims a life every minute. The story of Zee Pinkerton, a student and football player in Kansas, serves as a cautionary tale that TB is neither a disease of the past nor limited to poor countries, but something to be reckoned with in this day and age of 21st century medicine. On the upside, there is a growing global consensus that a simple blood test made by QIAGEN can catch TB infections long before they develop into a public health crisis.

It started with a cough that wouldn't go away. In this story, it afflicted a high school student in Kansas who played football, basketball and ran track. He sought medical advice and received numerous erroneous diagnoses until a physician finally fingered the culprit of his protracted malaise: a latent tuberculosis (TB) infection that had flared up into its active and highly contagious form. He was quarantined for months and struggled to resume his normal life long after his regimen of powerful medications had ended.

ZEE PINKERTON was an aspiring high school senior getting ready to graduate from Olathe Northwest High School near Kansas City in the spring of 2015. While recovering from a knee injury sustained during sports, he developed a mysterious cough, combined with night sweats and weight loss. The family physician treated him unsuccessfully for pneumonia. It took multiple doctor visits over the course of two months until a chest X-ray and a blood test confirmed that Pinkerton suffered from active TB.

"Oh man, it was really scary –
I didn't know
if I would live or die."

Pinkerton attends the University of Missouri in Kansas City, just across the state line. He knew that his biological mother had died from TB back in his native Ethiopia when he was only seven years old, but he had been vaccinated and undergone the standard skin test before being adopted by a U.S. family in 2007. "I had no idea I had carried the latent infection for all those years."

Like most children who are born outside of the U.S., Pinkerton had been vaccinated against TB with the bacillus Calmette-Guérin (BCG) vaccine as a child and was later tested with the commonly used 100-year-old tuberculin skin test called TST. However, the test never flagged his latent infection.

The traditional skin test's limitations point to a growing problem of how to best identify TB infections. Though only 10% of individuals infected with LTBI will go on to develop active TB, prevention is essential. Given the silent symptoms of LTBI, people like Zee Pinkerton often aren't diagnosed until the disease has progressed to the active stage, at which point it can explode into a public health emergency.

Responding to a global challenge

Hundreds of millions of people around the world have contracted a latent TB infection (LTBI) like Pinkerton and have probably lived with it for many years before it became an active and, at this stage, virulent infection. Tuberculosis remains one of the biggest infectious-disease killers worldwide, resulting in 1.6 million deaths in 2017 alone. In other words, TB claims a life every minute.

Approximately one in four people worldwide, including an estimated 13 million people in the U.S., are infected with LTBI, which exhibits no symptoms and can progress to the highly contagious TB disease, particularly in those with a compromised immune system.

In September 2018, the United Nations General Assembly convened its first ever high-level meeting on the fight against tuberculosis under the theme "United to end tuberculosis: an urgent global response to a global epidemic." The World Health Organization (WHO) in early 2018 issued new, updated guidelines on screening for latent TB infections, and the U.S. Centers for Disease Control and Prevention (CDC) Division of Global Migration and Quarantine has mandated the use of blood-based TB tests for more reliable immigration screenings.

Effective Strategy

Fighting TB in its early latent stage is crucial to prevent its spread, and effective testing is the most powerful tool available. By implementing the new CDC screening guidelines, stories like Pinkerton's can be avoided. That opinion is shared by Dr. Michael Lauzardo, a pulmonary disease specialist with the University of Florida Health system.

"With the increased precision of this blood test, you take the whole issue of vaccination out of the equation."

Studies have shown that mandating a blood test for immigration screenings is an "exceptionally effective strategy," Dr. Lauzardo points out. The skin test, in contrast, has its limitations, "particularly when used on patients who come from countries with historically high rates of TB infection." Testing the skin for an antibody response is less precise than a blood test, returning twice as many false positives for latent infections. "This can lead to people being put unnecessarily on medications, which consume public health resources and can cause side effects. Second, it gives patients who come from at-risk geographies and were vaccinated a false sense of security." And, as Dr. Lauzardo adds, people tend to shrug off the test, saying they expected a positive result anyway because they were vaccinated. "As a result, they don't seek treatment."

Pinkerton was quarantined at his family's house in Kansas for two months while health officials screened hundreds of students and staff at his high school, as well as his friends. Close to 50 students and his foster parents eventually tested positive for LTBI and received treatment, although no one else developed active TB like he had.

While Pinkerton was cooped up at home, he had to send his saliva to the Kansas Department of Health on a daily basis to be tested. It took two months before his sputum sample tested negative for three consecutive days and he was therefore no longer considered contagious. "Meanwhile, I sat on my porch and quickly ran out of things to do and books to read," says Pinkerton, "but what helped me was the amazing support from my community during that time."

Pinkerton took his active infection as the cue to become involved in pushing for better TB education. He joined the advocacy and survivor group "We Are TB" and has lobbied lawmakers for the need to fund more research into treating and vaccinating against the disease. "I'm not scared anymore," says the college student, who wants to get an MBA degree. "I've come to realize through my personal experience that TB is not a foreign but a domestic problem. And it needs to be tackled."

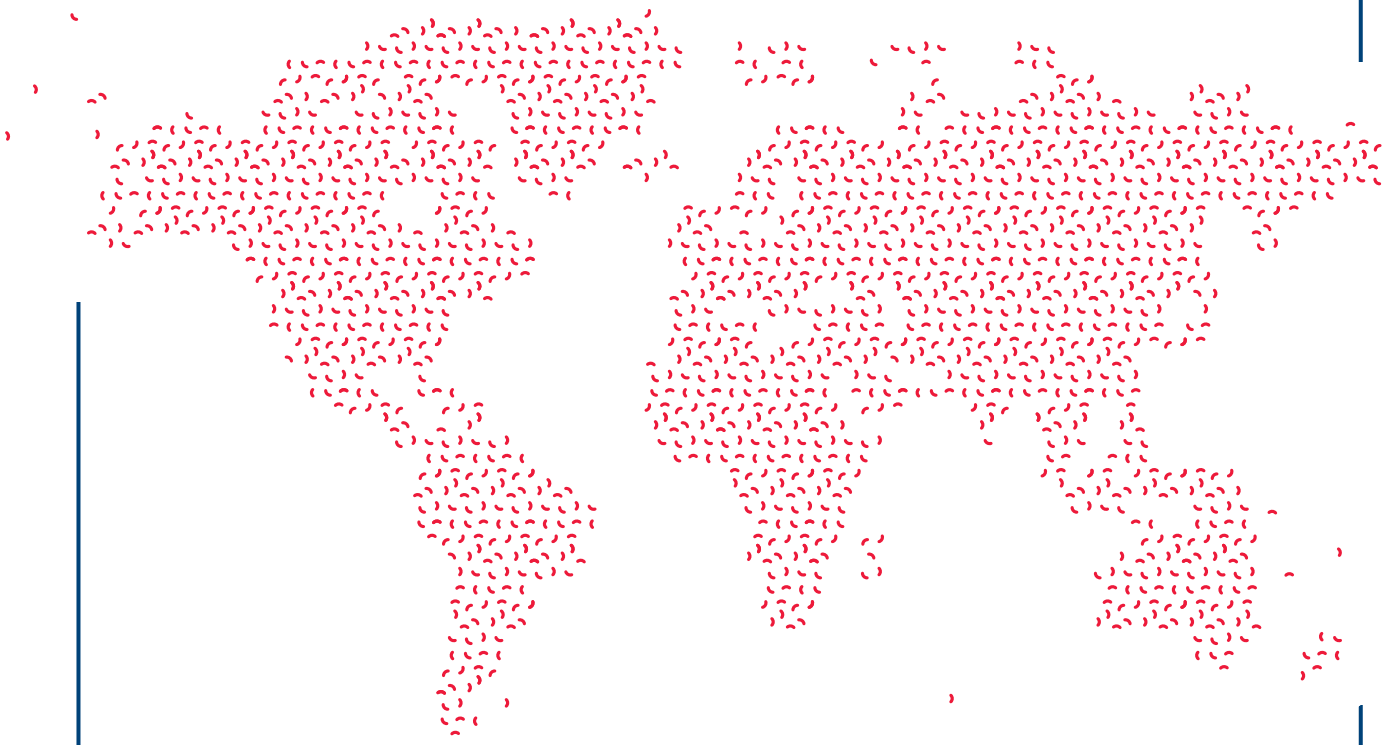
GLOBAL IMPACT OF TB

87%

of new TB cases in 2017 occurred in the 30 high-TB-burden countries. Eight countries accounted for two-thirds of new TB cases: India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh and South Africa.

LONDON – THE TB CAPITAL OF THE WESTERN WORLD

Tuberculosis isn't just a disease that harms people in so-called developing countries, even if 95% of all cases appear in those regions. In the Western world, London is the TB capital – with numbers comparable to countries like Rwanda or Guatemala. One-third of London's boroughs exceed the WHO "high incidence" threshold of 40 cases per 100,000 people, as a 2015 report from the London Assembly shows.



25%

of new TB cases occurred in the African region

62%

of new TB cases occurred in the Southeast Asian and Western Pacific regions

Source: Global tuberculosis report 2018, WHO

Homemade pipe bombs, courtesy of the local fire marshal, ready to be detonated for evidence collection.

A bomb explodes with a telltale boom, the blast forcing open the doors of a storage container and sending fragments scattering across the concrete outside. A group of scientists led by Dr. Sheree Hughes-Stamm uses brooms and bristles covered with protective paper to gather scraps and shreds into evidence bags in what is the preliminary step of DNA identification on really challenging sets of remains.

Minutes before, the county fire marshal has issued the command "Fire in the hole!" The crowd quiets and backs away from a LEGO-like structure of box cars about 100 meters away. The pipe bomb, freshly assembled on a truck tailgate, detonates inside one of the storage containers at this fire training facility in Conroe, Texas.

At the same time, **Dr. Sheree Hughes-Stamm**, head of the Forensic Biology Human Identification Laboratory at Australia's University of Queensland and a Senior Research Fellow at Sam Houston State University in the USA, and her students, dressed head to toe in bright white and yellow personal protective equipment (PPE), grab brooms and brown evidence bags, readying themselves to enter the metal container to start collection as soon as they are cleared to do so.

"These are tough types of samples to collect for evidence and identification," says Hughes-Stamm after the explosion, in a textured Aussie accent that lingers a bit on vowels. "When someone touches an improvised explosive device (IED), they only leave trace amounts of DNA to begin with. The heat from the explosion further degrades that DNA." The research of Hughes-Stamm helps in doing a better job of collection from the start.

"Minimizing any losses gives us, for instance, more to work with as we try to obtain a profile to help investigators identify the person who made the device." With such challenging samples, reliable identification becomes very difficult, sometimes impossible. "But by using different methods, starting with improving the way we collect information, moving to how we process the sample, and different ways of examining various genetic markers, we hope to provide more definitive identification, whether it's a person of interest in a terrorist attack, or the victim of a crime or a missing person case."

Hughes-Stamm waits while her students collect pipe bomb debris after a controlled detonation – the debris will later be analyzed for DNA.→

One of Hughes-Stamm's graduate students shows her advisor some pipe bomb fragments collected for DNA analysis.↓

It all started with a book

Once the evidence bags have been filled and cataloged, Hughes-Stamm sheds her goggles and white Tyvek jumpsuit, revealing shoulder-length black hair with flashes of reddish-purple underneath, and expressive brown eyes. Even in jeans and knee-high boots, she is much more glamorous than her research – and the ballooning PPE jumpsuit she formerly donned – might originally lead one to suspect.

Hughes-Stamm says she's always been fascinated with biology – as well as dissection and anatomy. But when it came time to choose her high school courses, uncertain what she wanted to do, she found herself at the library, perusing a display on different careers. "There was a book with a dead body and a crime scene marker on the front. I didn't even know what forensic science was at the time, but as soon as I opened that book, I was hooked."

One of Hughes-Stamm's graduate students waits as the local fire marshal fires his weapon, ready to pick up the shell casing for DNA analysis.↑

Hughes-Stamm did her undergraduate degree in anatomy, specializing in osteology, the study of human bones. She started her career in a forensic anthropology laboratory, helping to furnish investigators information about age, sex, and race of skeletal remains collected at crime scenes. But she felt limited by what information she could provide.

"I realized I needed a wider skill set," she says. "So I went on to do my Ph.D. in forensic genetics. It's allowed me to marry the things I love, anatomy and forensic genetics, so I can do DNA identification on really challenging sets of remains."

Harvesting as much genetic information as possible

Hughes-Stamm and her team had spent half the previous day at a shooting range in Huntsville, Texas. The researchers had two volunteers from the local fire marshal's office shoot ten rounds from five of their respective personal firearms as part of

Hughes-Stamm stands next to the donor cadaver that her team is studying at Sam Houston State University's Applied Anatomical Research Center (AARC) facility, otherwise known as the "body farm."←

Hughes-Stamm swabs one of the recently discharged firearms, in hopes of better understanding what collection conditions allow for a more complete DNA profile after analysis.→

research to investigate the best ways to collect touch DNA evidence. The students picked up each bullet casing, and swabbed the slides, triggers, and grips of each gun, planning to process the items back in the lab and compare the extracted information to buccal swabs taken from both shooters.

"We're testing out a new workflow to process this touch DNA. Since it's from a firearm, it's quite relevant – much like a gun you might find at a crime scene in the real world," explains Hughes-Stamm. "It's difficult to recover reliable DNA from a gun. Only a very small amount of DNA gets transferred from your hands to any touched item. And the heat from the gun damages and degrades the DNA, both on the gun and the bullet casing, making it even more difficult to get a good DNA profile."

Trace DNA from firearms isn't the only burdensome identification workflow that Hughes-Stamm's team is trying to improve. They are also interested in gleaning more information from less tissue from decomposing and skeletal remains. And so, later that afternoon, the team heads to the Sam Houston State University's Applied Anatomical Research Center (AARC) facility, one of the nation's few so-called "body farms," where researchers can study body decomposition and forensic techniques in a controlled setting.

The researchers have been taking collection swabs every few days from a willed donor cadaver laid out in the forest. As Hughes-Stamm bends down to take a new swab from the deceased's ankle, the bloated flesh coming off in delicate flakes, she mutters that people don't understand just how quickly bodies decompose.

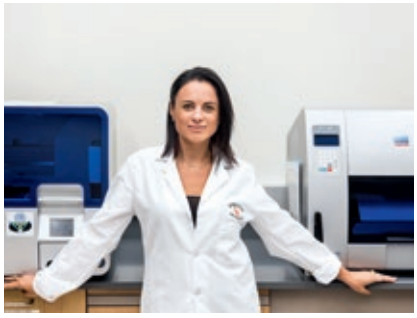
"It happens much faster than you might think. And as the tissues degrade, the DNA inside the cells in that tissue also become damaged. The more decomposition there is, the harder it becomes to get a really reliable DNA profile for identification."

Turning point for DNA identification techniques

This becomes a major issue in the event of a terrorist attack or mass casualty incident. With current techniques, if forensic facilities lose power and bodies or tissue can't be effectively stored, normal bodily decomposition can wreak havoc on a lab's identification capabilities. But, Hughes-Stamm says, if forensic scientists could find a way to rapidly collect swabs from the bodies, preserve them at room temperature for weeks, perhaps even months, before processing, they might be able to more efficiently handle identifications after events like the mass wildfires in California, tsunamis in Southeast Asia, or the terrorist attacks at the World Trade Center in New York.

"A big turning point for DNA identification techniques was the September 11 tragedy. Our existing technology couldn't handle such trace amounts of the highly degraded DNA that could be collected," she says. "It spurred the field to focus on the development and refinement of workflows to help us better identify degraded remains."

Back in the forensic science laboratory at Sam Houston State University, Hughes-Stamm credits QIAGEN for helping her team come up with these new and improved workflows. As one of her students loads the QIAcube with samples from the past two days' events to prep them for further analysis, she discusses the advantages of using the company's forensic genetics products.



"QIAGEN pretty much has a solution for everything," she says. "One of their strengths is being able to provide a solution in each area of the workflow – and since they take such a modular approach to those solutions, it's easy to switch them in and out so you can figure out what works best with particular applications."

"QIAGEN PRETTY MUCH HAS A SOLUTION FOR EVERYTHING."

SHEREE HUGHES-STAMM

Flexible workflow, robust chemistry

Hughes-Stamm asserts that what gives her and her team the freedom to investigate different collection and extraction techniques, particularly when it comes to DNA extraction, is the flexible workflow that QIAGEN provides, as well as their reliable, robust chemistry. That, she says, is how QIAGEN made their name in the field.

"We want to capture and collect as much DNA from a sample right from the start. With QIAGEN's depth of scientific knowledge and experience – it's really their cornerstone – we can better recover and extract DNA from our samples and process them directly to avoid any DNA loss."

She points to the company's short-tandem-repeat (STR) kits with quality sensors, as well as their DNA quantification kits and massively parallel sequencing (MPS) panel for missing persons as tools that support them in such endeavors.

"These are unique products to the field," Hughes-Stamm says. "And they provide the forensic community with answers to its problems by developing their products in collaboration with the market. They give us what we need to collect more DNA information from less and less of a sample – and that gives us even more opportunity to identify persons of interest in crimes, as well as missing persons or casualties."

When asked about her legacy, Hughes-Stamm tucks a flyaway tendril of hair behind one ear and nods toward her students, now working in the laboratory with the week's samples – extracting DNA from muscle, bone, and the dozens of swabs that were swept over bomb fragments, firearms, and bullet casings.

"My legacy really will be my students," Sheree Hughes-Stamm says, who, for the same reasons, is also QIAGEN's Young Investigator Ambassador for 2019. Her claim to this role she describes as follows: "Whether or not we can improve our methods to give us more information from smaller samples, identifying more people, solving more crimes, and bringing more closure – and I'm pretty confident we can – if I can guide my students to become leaders in the field and give them every advantage to make their careers phenomenal, that's enough for me. They are the superheroes of my research. And I can't wait to see what they do in the future."

QIAGEN ICMP Forensics Panel

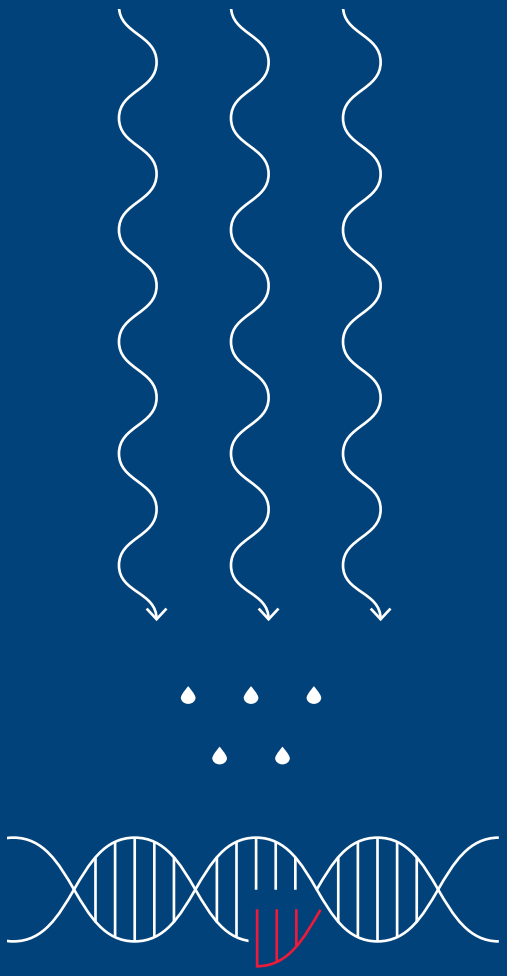
1,371
DNA markers in the panel

1,326
kinship markers

55
ancestry informative markers

5-10
cells of DNA for usable results

QIAGEN IS THE GLOBAL LEADER IN SAMPLE TECHNOLOGIES IN HUMAN IDENTIFICATION AND FORENSICS.

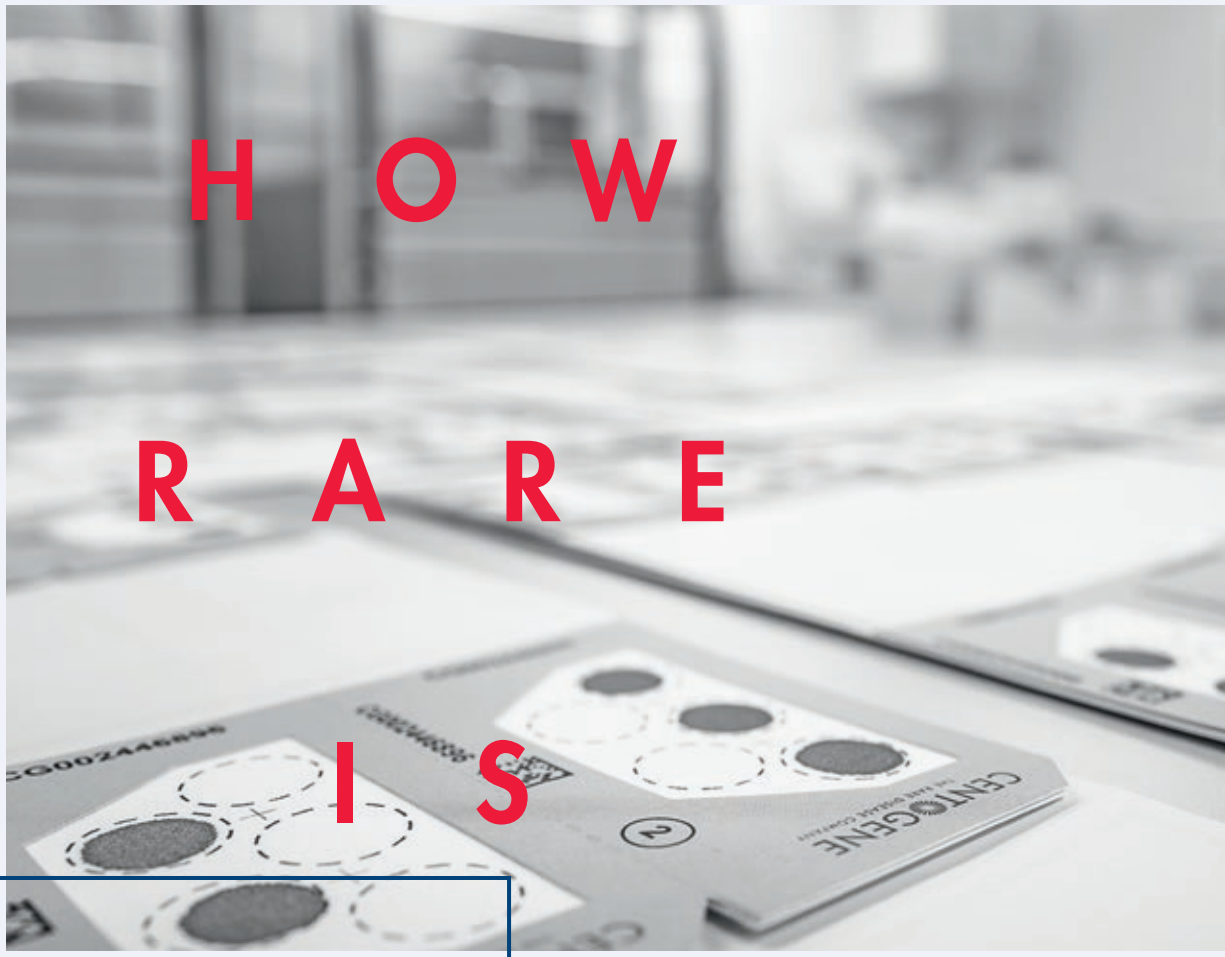


90 %

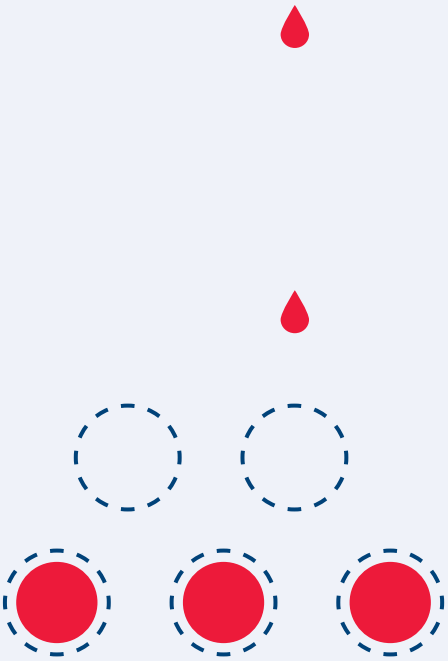
of the 8,000 victims of the Srebrenica genocide during the Yugoslav wars in the 1990s were identified by the International Commission of Missing Persons (ICMP). QIAGEN has partnered with the ICMP for many years in the development of novel molecular testing solutions used in this and many other complex missing persons scenarios in more than 40 countries.

HOW DOES DNA DEGRADE?

DNA can be damaged in a multitude of ways, including by UV irradiation, humidity, chemical damage, microbial digestion leading to physical or enzymatic breaks in the DNA, and much more. Problems can range from cross-linkages, or damage to or removal of bases, to single- or double-stranded breaks in the DNA double helix. The end result of cumulative amounts of DNA damage is DNA degradation – the breaking of DNA's long strands into smaller and smaller pieces. The more degraded the DNA is, the smaller the pieces, and the more difficult it is to generate a useful DNA profile. Testing solutions of QIAGEN can handle very degraded sample DNA.



HOW RARE IS RARE?



Every year, the company CENTOGENE receives thousands of postcards from all over the world – with drops of blood on every single one of them. Based on these samples, Dr. Arndt Rolfs, founder and CEO, has built an extensive database with genetic information on rare disorders. The collaboration with QIAGEN leveraged the world's largest hereditary disease testing database, making it widely accessible.

The decisive things are often those that can't be seen. This also applies to CENTOGENE's headquarters, located near the city harbor of Rostock, Germany: The impressive building's floor plan is shaped like a X chromosome, Mozart scores are printed on various glass walls that enclose the offices, and large photos – many of which were taken by the company's founder and owner, **Arndt Rolfs** – hang in the hallways. What aren't visible, but comprise the heart of the headquarters, according to Rolfs, are the data cables that reach from here to faraway Frankfurt am Main. → AR

ARNDT ROLFS "We store up to 30 terabytes of data per week on external servers in Frankfurt. In order to move this data securely within our own networks, it was necessary to lay a data line through six federal states, right up to the Main river."

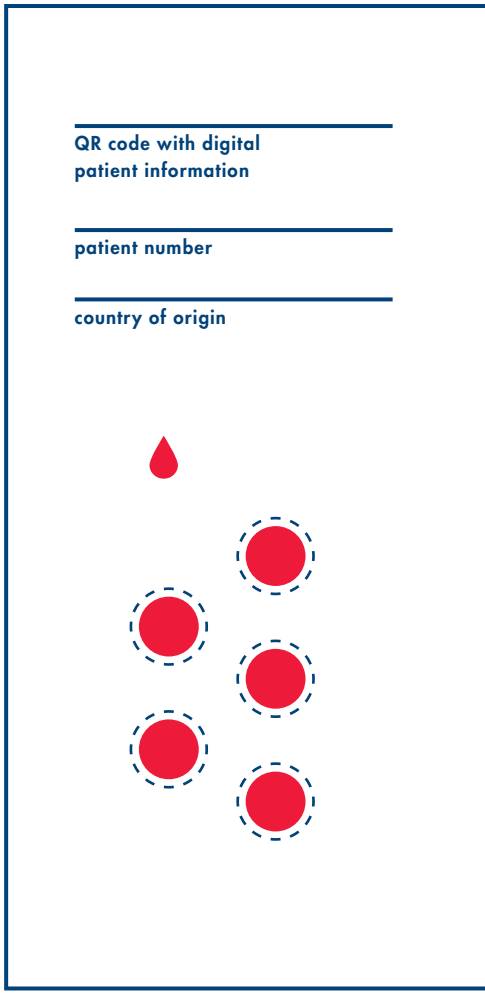
Arndt Rolfs has set up the world's largest database for rare hereditary diseases. It offers a unique repository of genetic, biochemical and clinical information gathered from around 350,000 consenting individuals for more than 3,500 diseases. The company also markets genetic tests for around 3,800 genes to exclude or confirm almost any form of rare genetic disorder. More than 5,500 such rare diseases are known in medicine – Fabry disease, for example, a metabolic disorder that increases the risk of stroke. →

"Our CentoMD platform brings together data from 350,000 patients, covering more than one billion variants, which helps in the diagnosis of rare diseases and increasingly allows conclusions to be drawn in all medical areas, such as oncology."

For many years, CENTOGENE has cooperated with QIAGEN, the world's largest provider of bioinformatics solutions, to ensure that this data reaches as many researchers around the world as possible. Initially, the cooperation was limited to the exchange of data within the Allele Frequency Community, a landmark initiative creating an extensive, high-quality and ethnically diverse collection of human genomes for data interpretation in research and clinical applications. →

"QIAGEN's knowledge-based products and its business relationships in clinical diagnostics, pharmaceuticals and biotechnology can be an interesting further anchor point for CENTOGENE in the global genetic testing market. There is a good perspective that this builds a nice common basis for expansion, especially in the North American market."

Arndt Rolfs describes his company as an IT-based organization for knowledge generation, which is based, almost ironically, on a postcard system that is as simple as it is ingenious. To illustrate this point, Rolfs hurries ahead of his visitors, taking the stairs two steps at a time. A slim man in his early fifties, his hair short and gray, he is clad in



Ingenious and simple – the CentoCard®

A treasure in IKEA boxes: 225,000 blood samples simply dripped onto a postcard are stored in CENTOGENE´s "archive." ↑

a black turtleneck sweater under a dark jacket – and he's always in a hurry. →

"Come on, come on..."

He strides toward a door, swiftly taps in a code, and steps into a notably unspectacular space. The "archive," which Rolfs presents with pride, is but a large shelf filled with IKEA boxes made of opaque plastic. More than 225,000 blood samples are stored there, having been – and this is the highlight – simply dripped onto a postcard made of special paper and then sent to Rostock. Here, too, the inconspicuous is the decisive factor: Without the CentoCard®, CENTOGENE would not exist in its present form. →

"They originate in Saudi Arabia, Pakistan, Mexico, the U.S., Nepal and many other countries. The oldest postcards have been stored here for almost 10 years now, yet the samples can still be used. We have proven stability for enzymes, biomarker and DNA for a minimum of 11 years."

Rapid growth

Arndt Rolfs founded CENTOGENE in 2006, giving up finally in 2018 his tenured chair at the Albrecht Kossel Institute for Neuroregeneration at the University of Rostock. The company has been growing at a great pace. It now has offices in Dubai, Delhi, Vienna, Berlin and most recently Boston/Cambridge, US. More than 350 employees from 40 nations work at the company's headquarters in Rostock, and they will soon number 450 – the new building already needs an extension.

Rolfs occupies a stylish and very tidy corner office. Beautiful black-and-white framed photographs lean against the walls like furniture, alongside a framed opera poster of *La Straniera*. A collection of rubber ducks lines the floor-to-ceiling

FIELD FOR BLOOD DROPS

Samples are punched out in the magnitude of one millimeter. Nucleic acids are chemically retrieved and analyzed. Mutations are then detected by Sanger or NGS sequencing. In parallel tandem mass spectrometry is done to analyze proteomic and metabolomics data sets, a simple, robust and very inexpensive method. Up to 9,000 different tests can be carried out using this postcard format.

Starting the DNA extraction from a blood sample. ↑

windows. Behind the windows, the Warnow river flows wet and gray, ending a few kilometers further downstream, where it flows into the Baltic Sea. There, on a sunny day at the beach, the prologue to the CENTOGENE story took place: More than 20 years ago, Rolfs was reading a weekly magazine on one of his infrequent days off when the physician first learned of a rare hereditary condition called Gaucher's disease. →

At that point, no one in Europe could diagnose the genetic and biochemistry basis of this disease. It took Rolfs and his team at Rostock University Hospital three months to develop the world's first test for Gaucher's disease. Rolfs had found a new life goal – and the patient, an answer to his previously unexplained ailments. He was one of the first to benefit from a new therapy developed by a U.S. company. In their business plan, the Americans had assumed a market of no more than around 60 patients worldwide for their treatment. CENTOGENE has diagnosed more than 1,000 cases of Gaucher's disease to date – and that's in Germany alone. The closer you look, the more you find. Data from CENTOGENE show that "rare" is more frequent than even experts assume. →

Rolfs, on the other hand, regularly finds new connections that he initially wasn't even looking for. The diagnosis of rare hereditary diseases now accounts for just under half of his company's sales. About 50% is generated through cooperation with pharmaceutical companies. A second data platform for this business, CentoPharma®, was launched in 2018. →

Orphan drug-developing pharmaceutical companies can retrieve original anonymized real-life data, genotype–phenotype, clinical information, frequency of special mutations and global epidemiological data from CENTOGENE, originating in more than 115 countries, based

ARNDT ROLFS "Chance would have it that the following day a patient with unexplained epileptic seizures was presented to me at the Department for Neurology in Rostock. I had the feeling that the patient would describe his symptoms in the same way as the article I had read about Gaucher's disease the day before. I asked more and more detailed questions, inquired about his bone pain, and couldn't help but submit to my astonished colleagues at the end: 'In my clinical experience, in this case I wouldn't eliminate Gaucher's disease.'"

"Rare diseases occur much more frequently than the current doctrine indicates. For Fabry disease, for example, the specialist literature mentions frequencies of one case per 60,000–100,000 inhabitants; according to our figures, the frequency is around one case per 13,000. This epidemiological fact applies to almost all of the rare hereditary diseases we're investigating. They are rare mainly because no one knew how to find them or did not think to look for them."

"It is unique – the world's first platform for targeted cohort identification."

Ready for the lab – more than 650 samples arrive at CENTOGENE each day. The turnaround time for an analysis is around 16 days. ↓

on desired geographical region-suspected or -confirmed diagnoses. Rolfs intends to establish new business areas through these latest collaborations, services such as therapy monitoring in addition to diagnosis, or by taking part in the development of new active substances. →

In addition, this know-how could be transferred from rare to common diseases that involve a hereditary factor, such as high blood pressure or certain types of cancer. A further focus in the evaluation of the data is on ethnic differences, another area that has received little attention so far – just because hardly anyone is looking at it. →

"We are developing, for example, an easy-to-measure biomarker at the protein level for every rare hereditary disease to offer a prognosis for the therapy concept and monitor the success of the treatment. It is sufficient for patients to send us regular blood samples on the CentoCard. By way of an app, after they receive our results on their smartphone, for instance, we can tell them whether the medication's dosage is well adjusted."

"It is overlooked far to often that people react differently to drugs depending on their genetic origin. The 'one pill for all' does not exist, because giving it to patients in Pakistan, China, the U.S. and Germany yields quite different results in effectiveness. We therefore see a further growth field in the ethnic interpretation of our data."

> 20 million
knowledge base findings

> 1 million
samples analyzed

> 35,000
publications

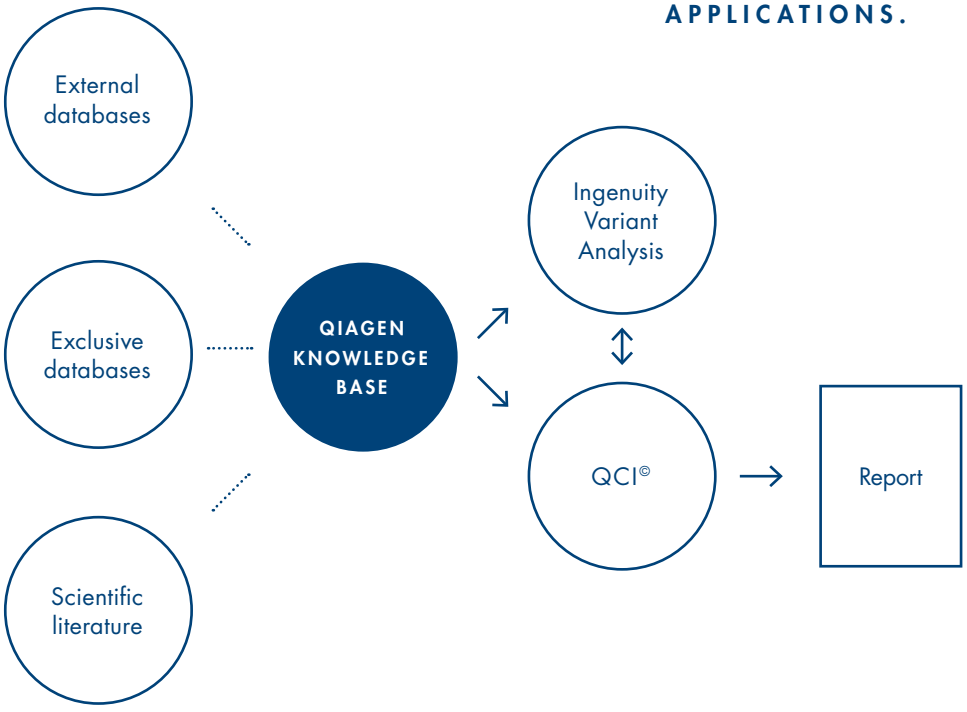
> 33,000
disease classes

> 35
integrated databases

> 5,500
new data elements and findings per day

QIAGEN IS THE WORLD'S LEADING PROVIDER OF BIOINFORMATICS SOLUTIONS FOR RESEARCH AND CLINICAL APPLICATIONS.

QIAGEN bioinformatics solutions for rare diseases



JAVERIA ABBASI (AGE 3 MONTHS), PAKISTAN

Javeria has been unable to drink much breast milk since birth, and has grown increasingly sleepy and apathetic. Sometimes, when awake for any extended period, she suffers from seizures with a tendency to opisthotonus, an involuntary backward arching of the head and overstretching of the arms, legs and trunk. After such a seizure, the little girl is very weak and requires a lot of physical closeness. "I hold her in my arms for hours," says her mother. "You can see how she recovers from the exhausting cramps." Initial examinations showed increased levels of leucine, isoleucine and valine. The test results confirmed the doctors' suspicion that it was maple syrup urine disease.

MAPLE SYRUP URINE DISEASE

The autosomal recessive hereditary disease also known as leucinosis causes disturbances in the metabolism of the branched-chain amino acids leucine, isoleucine and valine. These amino acids and their degradation products increasingly accumulate in the patient's blood and urine. This can lead to blood sugar deficiency and the inhibition of myelinization. If the disease remains undetected, severe permanent brain damage can occur, even in the first few days of life, and if left untreated, leads to death within a short time.

A liver transplant can make it possible to break down the branched amino acids by oneself. However, the availability of donor organs is very limited, especially for children, which is why conservative therapy must be used, by refraining from taking up branched amino acids in the diet.

Serving patients in a holiday resort – Arndt Rolfs with his team at a tour to diagnose patients in Nepal.↑

AHMAD RIZWAN (AGE 7), PAKISTAN

Ahmad has difficulties simply holding a pen. His mother noticed the first abnormalities in Ahmad's behavior when he was just five months old. At three and a half, he still couldn't speak and often stumbled or fell. When he was four, Ahmad had problems climbing stairs and getting to his feet. It was not just the strength in his legs that faded. One morning, Ahmad struggled to lift a pile of comic books onto the top shelf of his bookcase, but his arms were too weak. The seven-year-old likes to go to school, although his classmates have to help him climb the stairs and he often plays alone. Ahmad's dream is to play cricket with his friends. Ahmad has been diagnosed with Duchenne muscular dystrophy.

DUCHENNE MUSCULAR DYSTROPHY

This genetically determined synthesis disorder of the muscle protein dystrophin leads to muscle fibers being broken down and replaced by fat or connective tissue. Due to the X-chromosomal recessive inheritance, virtually only boys are affected. So-called "gnome calves" or "ball calves" are also characteristic, caused by fat deposits in the lower leg muscles.

Breathing and heart muscles are also affected in the late phases of the disease, which makes it more difficult to expectorate in the case of infections of the airways. This can considerably reduce life expectancy.

AT HOME IN THE WORLD

To collect data from many genetic origins, CENTOGENE created a network of more than 20,000 physicians. Arndt Rolfs also regularly travels to countries such as Nepal or Pakistan, including more remote areas where people have little or even no access to modern medicine.

In 2018 CENTOGENE initiated two big projects in these countries. In Pakistan, CENTOGENE cooperates with the largest children's hospital in Asia, based in Lahore. in Nepal, these structures are missing, but CENTOGENE booked several rooms in a hotel just outside of Kathmandu to serve as a medical base. On this island popular with tourists, Rolfs and his team diagnosed people from the Nepalese capital and its surroundings for a week. The conference room at the Mirabell Resort Hotel was converted into a waiting room, while the patients' medical histories were recorded in an adjacent hotel room. Blood was dripped onto the CentoCards and the team returned to Rostock with a large pile of samples to examine.

Rolfs is in the process of documenting the many patient stories from all over the world, intending to create a book from it. Parents often continue to search for answers many years after their children are born because they remain undiagnosed. Finally identifying the reason for their suffering helps them to live with the situation, but it is not enough to solve it. Therapies for rare diseases frequently cost as much as US$100,000, which is simply out of reach for these families. Rolfs and his teams continually strive to find new avenues to obtain treatment options for these patients.

ON THE BRINK OF A BREAK-THROUGH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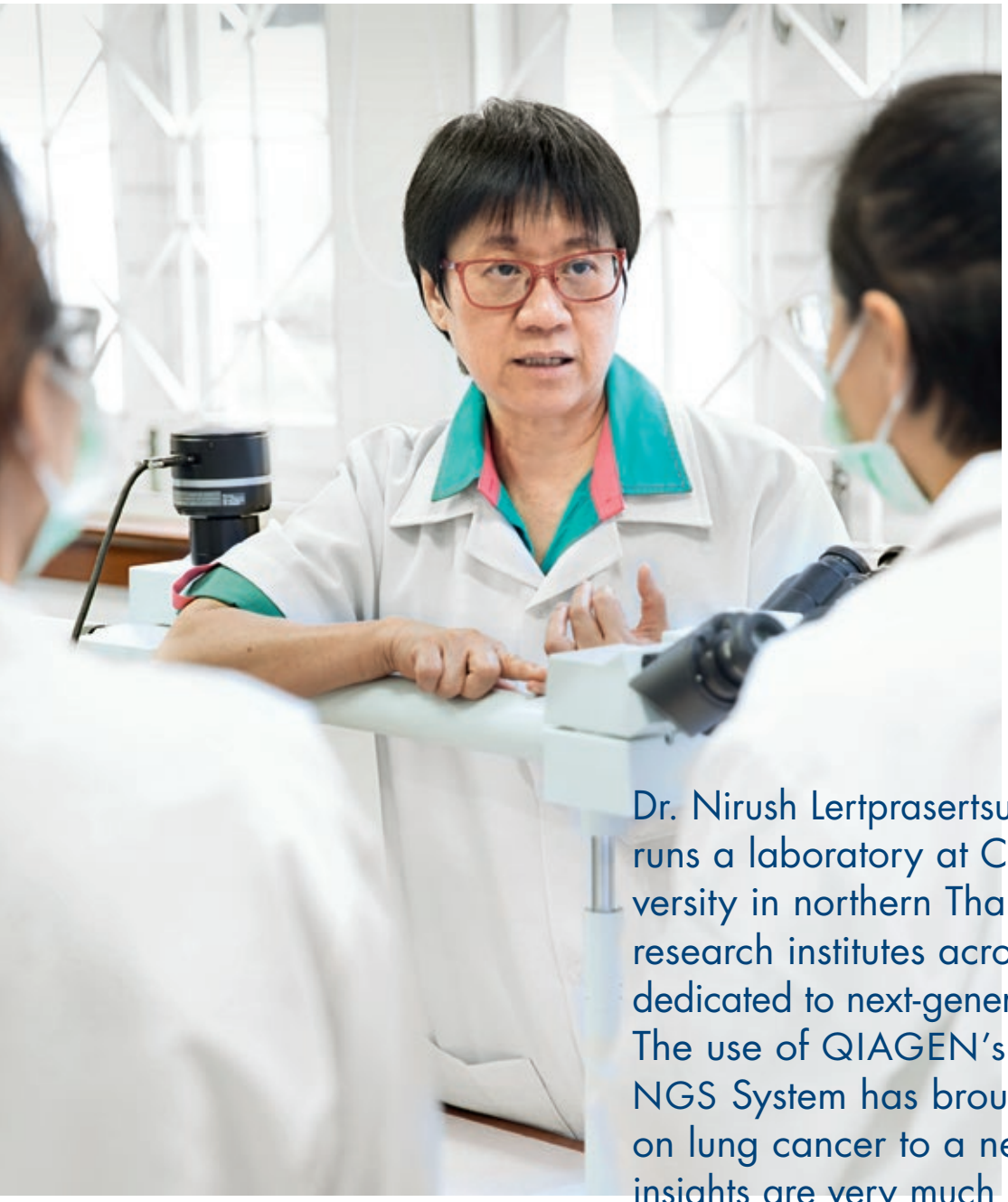


Dr. Nirush teaching in the pathology lab at Chiang Mai University. She has been mentoring young researchers for 26 years. ↑

Dr. Nirush Lertprasertsuke, a pathologist, runs a laboratory at Chiang Mai University in northern Thailand, one of five research institutes across the country dedicated to next-generation sequencing. The use of QIAGEN's GeneReader NGS System has brought her research on lung cancer to a new level. And insights are very much needed, because the prevalence of the disease is almost four times higher than in other regions – and the reasons why are still in the dark.

Within minutes of showing up at her lab, associate professor **Dr. Nirush Lertprasertsuke** is surrounded by colleagues, doctoral students and staff. Patient case files and research must be reviewed, and papers have to be signed. All before Nirush, an anatomic pathologist at Chiang Mai University, hunkers down for a two-hour meeting with the hospital's surgeons and oncologists. They will discuss the area of research closest to Nirush's heart: the prevalence of lung cancer in northern Thailand. Currently, more than 40 of every 100,000 people are being diagnosed in this region annually. The reasons remain mostly unknown.

Slightly built, Nirush looks younger than her years. With a gentle yet resolute manner and an easy laugh, she is hands on in her work, keeping a stash of crisp, white lab coats in her office to change into before important meetings. Her professional discipline, she sees, is experiencing an important transformation. "New technologies are changing the world for us pathologists," she says. That is most notably true in her research for next-generation sequencing (NGS).

> **"COLLABORATION AND EXCHANGE ARE THE KEYS TO SUCCESSFUL RESEARCH."**
>
> **DR. NIRUSH LERTPRASERTSUKE**

The hospital laboratory recently acquired a QIAGEN GeneReader NGS System. The world's first truly complete NGS workflow combines all that is needed to go from a biological sample to actionable insights and reports. It transforms the clinical research of scientists like Dr. Nirush by providing deep, valuable insights on the genetic drivers of diseases in a cost-efficient and easy-to-use workflow.

Golden domes of ancient pagodas

At first glance, Chiang Mai hardly seems to be the place for cutting-edge research. The sleepy city in the green hills of northern Thailand was founded in 1296, where, in some corners of the old town at least, time seems to have stood still for centuries. The air is rich with the scent of the frangipani trees that line the city's alleys. The golden domes of ancient pagodas tower over small streets in which a mere 130,000 inhabitants live a quiet life.

The university hospital exudes a faded 1950s grandeur, where students walk on cream-colored terrazzo floors and open brass-handled windows to allow a cool breeze to enter. The medical school, where Dr. Nirush teaches and does research, is the largest in Thailand's northern region and acts as the pathology and molecular science referral center for all regional hospitals. A member of the Northern Thailand Oncology Group (NTOG) and the National Cancer Guidelines Committee, Dr. Nirush focuses on lung and gastrointestinal cancers.

Genetic factors at play

There are indications that the high concentration of the radioactive gas radon in the mountainous regions could partly explain why the incidence of lung cancer is so high. Genetic factors are also at play. "In Asians, an estimated up to 55% of lung cancers are triggered by driver gene mutations," says Nirush. To find those mutations, the GeneReader offers a wide array of genome-sequencing panels to identify more than 1,250 gene mutations in one tumor sample. This so-called GeneRead QIAact AIT panel is the core assay for the QIAGEN's NGS system – it targets up to 30 clinically actionable genes that are often analyzed in most prevalent types of cancer.

Dr. Nirush says that the GeneReader workflow has "a strong input" into her research, because it reports findings that can really have an impact. "Now that we can find the mutation that caused that particular cancer to grow, we can work on targeted, specific therapies." Therapies that are less costly, more promising and more convenient for the patients.

Five laboratories are dedicated to next-generation sequencing across Thailand today, including Dr. Nirush's lab. "We are working closely with oncologists, thoracic surgeons, and GI and HBP surgeons in Thailand's northern region, as well as collaborating with pathologists and molecular scientists in Bangkok and across Southeast Asia."

"PEOPLE DEAL WITH MUCH MORE THAN JUST THE ILLNESS. THE CIRCUMSTANCES PUT A LOT OF STRAIN ON EVERYONE."

DR. NIRUSH LERTPRASERTSUKE

Up to 55% of lung cancers in Asia are triggered by driver gene mutation.↑

Dr. Nirush and her colleagues are eager to put the GeneReader to good use, believing that Chiang Mai, located in the heart of Southeast Asia at the crossroads of successive waves of migration, could prove the perfect city for genome-based cancer research. Hill tribes in the mountainous northern and western regions, Malays in the south, and Arab, Indian and Chinese immigrants have all contributed to a rich gene pool that could hold the answers to urgent questions, says Nirush, who traces her own ancestry to Chinese migrants.

Cancer afflicts the whole family

Working in a city surrounded by farmland fuels the sense of urgency she feels when she looks at the possibilities that targeted cancer therapies offer. "In a country like Thailand, cancer often afflicts the whole family. When we use regular treatments, like hospital-administered chemotherapy, at least two relatives must take turns staying in hospital with the patient at all times," says Nirush. "It is expected that the family feeds and cares for the patient."

Working family members often have to quit their jobs or leave the farm to care for a loved one. Children are regularly sent far away to be cared for by other family members. These difficulties come on top of the medical challenges presented by chemotherapy itself. "People deal with much more than just the illness. The circumstances put a lot of strain on everyone," Nirush points out, adding that a new generation of medicine that can be taken at home will ease the burden for families and at the same time be far more cost effective. "We can do a lot of good there."

And she is not doing it alone, because Thailand has a small but quite active community of cancer researchers. Dr. Nirush's findings on cancer research are widely published, and she collaborates with colleagues from other Thai universities and those overseas. "Collaboration and exchange are the keys to successful research," Nirush says. Accordingly, she has established an informal network and set up many scientific platforms, including inter-hospital conferences, a scientific congress and a joint symposium to exchange experiences within groups and clinicians. "A further ambitious plan is to set up a study center in the near future," the scientist says, adding that hopes of comprehensive genomic profiling of patients will help acquire more data and enable them to gain a deeper understanding of the "emperor of all maladies."

The GeneReader NGS System is situated in an air-conditioned space in the Pathology Lab at Chiang Mai University, helping to prevent samples from being spoiled by the tropical heat.→

GeneReader NGS System

- Fully integrated workflows
- Actionable insights
- Flexibility to fit customer needs
- Guaranteed results with predictable costs
- Expertise and service from one point of contact

THE GENEREADER NGS SYSTEM IS THE ONLY INTEGRATED NGS WORKFLOW THAT TAKES USERS FROM SAMPLE TO ACTIONABLE INSIGHTS.

SEA CHANGE IN ONCOLOGY

Immunotherapy, a host of methods in which doctors harness the body's immune system to fight cancer, is turning the tide in the treatment of cancer. We met with scientist Nathalie Labarrière, from the National Health and Research Institute in Nantes, France, for whom this has been the subject of research for almost all of her scientific career.

Nathalie Labarrière, a biologist and immunologist by training, peers into a microscope. Next to her sit plastic trays about the size of a paperback book, their surfaces dotted with small wells filled with a pinkish fluid. They are stacked high in an incubator, an oven-like device to multiply cells – T-cells in this case, a part of the immune system, and the subject of Labarrière's research. Her topic has recently become one of the hottest in oncology: immunotherapy.

Behind immuno-oncology (I-O), what some call a revolution in cancer therapy, lies a straightforward, even simple premise: the manipulation of the immune system's T-cells, enabling them to recognize tumor cells – and kill them.

The concept that tumors can be attacked by activating the patient´s immune system dates back more than 20 years, but most recently, when the Swedish Academy of Sciences awarded last year´s Nobel Prize for medicine to James Allison, of the University of Texas, and Tasuku Honjo, of Kyoto University, it became clear to everyone that I-O was destined to become one of the most promising approaches in cancer therapy in this day and age. The research of Allison and Honjo has already led to the successful development of new immunotherapies, giving hope to many patients all over the world and creating a multi-billion-dollar marketplace.

QIAGEN, from the beginning, has been an important partner of pioneers like James Allison and Tasuku Honjo. Today, scientists search with QIAGEN sequencing technology for new biomarkers and antigens, or use next-generation sequencing and the huge QIAGEN databases to develop new drugs, on to the application in hospitals, where physicians trust reports with actionable insights generated by QIAGEN's clinical-decision support solutions.

"IT'S THE BEGINNING OF A REVOLUTION."

NATHALIE LABARRIÈRE

Perfect model to study I-O

Nathalie Labarrière is using QIAGEN's T-cell receptor kit and targeted RNA panels at the National Health and Research Institute in Nantes. Housed in a steel- and glass-clad building nestled on the banks of the Loire, it calls to mind a ship lying in dock.

Her work on immunotherapy started in 1995 with a number of clinical trials, when she became interested in tumor immunology, mostly focusing on melanoma, a cancer of the cells responsible for skin pigment and well recognized by the human immune system – making it a perfect model to study I-O.

In her research she is using multiple datasets which, overlaid together, give a comprehensive picture of I-O. T-cell receptors are just one aspect of the puzzle – adding in gene expression to monitor PD-1 and other related genes is another piece of the puzzle. "My research targets ways to monitor the immune responses of cancer patients treated with anti-PD-1 antibodies, as well as the best selection of T-cells for adoptive cell transfer," Labarrière explains. She and her team analyze the many different proteins on the surface of T-cells. QIAGEN's T-cell receptor kit helps them to find certain markers that can identify which patients are most likely to benefit from immunotherapy, and to decide if a patient will be among those who respond to an immunotherapy treatment, or who may be in danger of a relapse.

Immunotherapy has a positive effect on some but not all patients. "Anti-PD-1 therapy, for instance, helps fewer than half of cancer patients," Labarrière says. Finding early and robust predictive markers of clinical response therefore improves patient management and reduces costs. Furthermore, the comprehensive analysis of PD-1 regulation and signaling will also have a considerable impact on

the optimization of other immunotherapies, such as T-cell-based immunotherapies.

Needles in haystacks

What researchers like Nathalie Labarrière seek are often needles in haystacks. Each immune system is unique, and needs to be genetically defined. Of the T-cells alone, more than 10,000 different species exist in the blood, all of which have different functions. And of these, one must be identified that reacts to the tumor's specific genetic version.

To help researchers gain better and faster insights, in 2018 QIAGEN launched its first applications specially developed for use in I-O. The new QIAseq tumor mutational burden (TMB) targets variants in 486 genes, covering full exons. The new panel generates data with higher sensitivity and lower requirements for DNA input 01 including further improvements to its QCI Interpret´s somatic-cancer clinical-decision support. 02

Nathalie Labarrière is convinced that the research community is experiencing "the beginning of a revolution." She foresees that a lot of things are going to change, and patient outcome will improve. Knowing that her team's hard work could be part of a sea change in oncology to save more lives is, she says, "the biggest motivation."

QIAGEN OFFERS KEY BIOMARKERS FOR I-O RESEARCH, AND PARTNERS WITH PHARMA TO PROVIDE COMPANION DIAGNOSTICS FOR I-O DRUGS.

QIAGEN in immuno-oncology

GENE PANELS: QIAGEN offers a broad range of assays which analyze key biomarkers that indicate the likelihood for patients' response to I-O drugs. They include gene expression assays covering up to 1,000 genes and panels for immune repertoire monitoring, as well as the QIAseq TMB panel, which measures tumor mutational burden and microsatellite instability.

COMPANION DIAGNOSTICS: QIAGEN provides key biomarkers and novel gene expression profiles for I-O research and is partnering with pharma companies such as Bristol-Myers Squibb.

BIOINFORMATICS: QCI, QIAGEN's bioinformatics solution to interpret sequencing data from clinical samples, shows patients' biomarker status for I-O response.

01 WITH 40NG DNA the workflow can proceed with less than a whole exon. Like other QIAseq workflows, the panel incorporates unique molecular indexes (UMIs), tagging every molecule in a sample at an early stage to eliminate errors and produce higher quality.

02 THE APPLICATIONS help doctors and researchers with interpretations and reporting of TMB and MSI using QIAGEN's CLC Genomics Workbench.

03 CAR stands for chimeric antigen receptor which is used in another form of immunotherapy. The molecule is added to the T-cell so it can recognize formerly invisible cancer cells.

BLOCKING THE DEACTIVATION

The signals of PD-L1 in immunotherapy

2. INTERACTION
The protein PD-L1 (the programmed death ligand) docks at a T-cell and interacts with cancer cell receptors like PD-1.

3. REACTIVATION
The antigen anti-PD-L1 blocks the interaction between the receptors PD-1 and PD-L1, uncovering the tumor cell and making it visible to the T-cell – which starts its mission to attack the malignant cell.

1. TAKE COVER
A cancer cell can mask itself by manipulating so-called checkpoints of our immune system, for instance by producing PD-L1 (programmed death ligand) to block the activity of a T-cell.

THE LENGTHY BEGINNING OF A REVOLUTION

1980 Nobel Prize winners James Allison (University of Texas) and Tasuku Honjo (University of Kyoto) start basic researches in immunotherapies.

2010 Patients with incurable chronic lymphocytic leukemia were successfully treated for the first time. In two of these three patients, the tumor completely regressed within four weeks.

2012 The first child received therapy and is still cancer-free today.

2017 The first therapies with CAR 03 T-cells, Kymriah and Yescarta, were approved for use in the U.S., one of which subsequently received E.U. approval.

2018 QIAGEN expands NGS portfolio with first immuno-oncology panels

A FLYING VISIT ...

WITH QIAGEN ASSOCIATE AMADOU GUEYE IN KAMPALA, UGANDA

"WE REALLY MAKE AN IMPACT ON LIVES IN AFRICA."

Amadou Gueye, market development manager for Sub-Sahara Africa, has just arrived in the Ugandan capital of Kampala on the first early morning flight from the neighboring country Rwanda. He is here visiting the International Organization for Migration (IOM), a United Nations agency for the resettlement of refugees and migrants, to investigate why one of the machines used to test for latent tuberculosis is malfunctioning. This is one of nine TB test devices QIAGEN has installed in Africa for the IOM. The fates of thousands depends on these machines functioning properly, since these test results are one of the last requirements by western governments before refugees are granted entry. Just outside the door at the Kampala IOM, Somali and Rwandan families await their test results with their suitcases packed.

Gueye consults with Moses Mwesigwa, IOM's chief laboratory technician, over a malfunctioning robot arm designed to handle test liquids. Just a few months earlier, Gueye trained Mwesigwa and they installed the device together. After checking over the equipment, monitoring a few practice runs, and cleaning every single component, the machine works again.

"MY GOAL FOR THE NEXT FIVE YEARS IS TO ESTABLISH OUR QUANTIFERON-TB SOLUTIONS AS THE STANDARD OF CARE FOR LATENT TB DIAGNOSIS ON THE AFRICAN CONTINENT."

Many problems in labs around the world can be solved via a QIAGEN telephone hotline, but in Africa the culture is different – people turn to other people whom they know. That's why Gueye is willing to travel as much as he does, knowing how important face-to-face meetings are for his African customers. On this trip to Uganda, he has set up a meeting with officials from the country's national TB program in order to introduce QuantiFERON into their test algorithms. The next day, Amadou will fly on to South Africa.

"I EXPLAIN TO MY KIDS THAT I HELP DOCTORS IN AFRICA UNDERSTAND WHY PEOPLE ARE SICK."

QIAGEN cooperations with IOM in latent TB testing

Every two weeks Amadou Gueye flies back and forth between his home in Paris and the African continent – he's been to 35 cities in the past 10 months alone. Every time Gueye gets on a plane, his 10-year-old son puts a pin into a world map to mark his father's next destination. For his job at QIAGEN, he is often ready to travel to places where nobody else wants to go. He recently spent two days traveling to a refugee camp in Makere, Tanzania, where he helped restart the testing process for latent TB using QuantiFERON.

QIAGEN PROVIDES ACCESS TO HEALTHCARE AND RESEARCH PRODUCTS THROUGHOUT THE DEVELOPING WORLD.

In a new partnership with Ellume, an Australian market leader for high-performance digitally enabled diagnostics, QIAGEN is developing a new testing solution: QuantiFERON®-TB Access is designed to pair ultrasensitive digital detection of latent TB infection with a complete workflow created with a focus on cost efficiency and ease of use to detect latent TB infections in low-resource, high-disease-burden countries. Clinical trials for QFT Access are planned to start in 2019, and commercialization is expected to begin in 2020.

In cooperation with PATH, an NGO, and support from the Bill & Melinda Gates Foundation, QIAGEN developed the testing system *care*HPV for use in regions with limited healthcare resources. This is an adaptation of our gold standard *digene* HC2 for detection of high-risk human papillomavirus (HPV), which has been shown to be the primary cause of cervical cancer.

> 25
countries worldwide offer *care*HPV

> 3 million
*care*HPV tests distributed since launch through the end of 2018

SERVICES FROM A SINGLE SOURCE

Skilled, committed and dynamic – a visit to the QIAGEN Service Center in Wroclaw, Poland.

The first thing you notice when visiting the QIAGEN Service Center in Wroclaw, Poland, is the feeling: The place exudes atmosphere. It has a groove, an energy, a remarkable liveliness.

More than 500 people move about the huge office, which resides in a modern building with a shopping center on its ground floor and a gleaming office tower above. The employees are passionate experts in IT, marketing, design or accountancy, many are seated at long rows of desks, in front of their computers; some are engaged in lively discussions in small groups in one of the colorful kitchens, while others are on the phone, in the corridors, slouched on sofas. On the floor above, a group of young men play FIFA in a cozy corner on a big screen. Startup atmosphere at its best.

In Wroclaw, QIAGEN brings together services from all over the world, such as accounting, marketing and IT, including the technologies and know-how needed to redesign the company's new website.

When the site was founded in 2012, no office existed, not even a handful of employees. None of them had heard of QIAGEN before. There isn't even a Q in the Polish alphabet. Nevertheless, the story of QIAGEN in Poland is written in a remarkable way. That's for three main reasons:

1 The location itself

The city's universities, with more than 150,000 students, provide well-trained, highly qualified graduates. Wroclaw also offers quality of life, a charming old town, and cosmopolitan, creative and engaging minds, not to mention the surrounding mountains, forests and lakes. No surprise then that word has gotten out about the attractiveness of the fourth-biggest city in Poland. More than 100 international corporations have settled in Wroclaw as Service Centers, and rent more than one million square meters of office space there. The practice of outsourcing services that don't belong to a company's core business is an effective strategy that has been used for a long time in the business world.

2 From start to finish

The Service Center in Poland is not a matter of offering services at a lower price, but of making them more efficient, of higher quality, scalable and more innovative by concentrating all of them in one place. Only services from a single source offer the opportunity to standardize, to automate and digitalize, or to even think, in new ways. In the future, Malgorzata Karpinska – senior manager with a degree in polytechnic studies, and just called Maggie by her colleagues – wants to develop further services, perhaps not only to process the invoices but take on the assignment as well. "We'll be even more cross-functional, and dissolving silo thinking. We can do this because QIAGEN gives us the possibility to shape and improve our processes and influence them."

3 The people

Well-trained people expect that same approach today. They want a challenging job; not just boring, repetitive work but something stimulating in terms of content. And the demand for qualified experts – mostly with extraordinary IT and biotechnology knowledge – is accordingly high, because of reason #1 above. In this competition, QIAGEN rivals major international banks and technology groups. The fact that QIAGEN can stand its ground and lure so many highly qualified applicants is because of reason #2. That is why the workforce in Wroclaw works every minute of the day with great passion and expertise – creating the special energy of the site. Three of these 500 employees give their own explanations on the coming pages.

Mari-anna

Marianna Dudzinska, Marketing Manager – Cycling and cross department cooperation

By training, I am a biologist – the reason I became a manager in marketing is because working with people is what keeps me inspired and motivated. Luckily, our company provides the opportunity to develop both professionally and personally and supports us with various sport activities such as MTB, running, basketball, volleyball, and even founding training groups with professional trainers. For instance, I'm thrilled to be riding MTB marathons with QIAGEN's BIKE Team.

Our marketing team is a diverse group of people with outstanding skills, special know-how, and a unique passion in addition to our work. We are responsible for various projects. Currently, Technical Product Excellence colleagues are working intensively together with global product managers to launch new panels and rebrand the QIAstat-Dx product line. Event Managers are focusing all of their energy on organizing the biggest conferences planned for 2019, like AACR and ECCMID, to make them as successful as possible. Design managers make sure that all projects run according to the QIAGEN brand.

Privately among us we have beer brewers, pilots, personal trainers and nutritionists. On the one hand, we are all very different, but on the other, we complement each other perfectly; professionally, but also with regard to our interests and characteristics. Everyone is highly motivated. It's really fun to work together.

MY BIGGEST CHALLENGE

We are a young team, a young organization – under a continuous process to define our autonomy and structures. It gives off a vibe of constant movement, flexibly and creatively. It's enthusiastic, but it might be a challenge for new employees to find their place in the company and adapt to the processes. That's why we're putting in effort to build a friendly work environment and better illustrate what QIAGEN is about. One such example is the DNA and instrument workshops where employees are invited to isolate their own DNA using our kits and devices, regardless of where they're working, from accounting to web design. It is great experience, because our colleagues immerse themselves in our product world in an almost playful way, and it enables us to move even closer together as one big team.

Maciej

Maciej Fojtar, IT Analysis Manager – A bridge between business and IT

I run a team of eight people. Right now our main focus is the Atlas project, the complete redesign of the company's website. We're talking about a few thousand pages and products, all of which have to be coordinated in order to work on different browsers, and of course on mobile devices. We work with Scrum methodology that gives us the flexibility and readiness to adjust to rapid changes in the business environment.

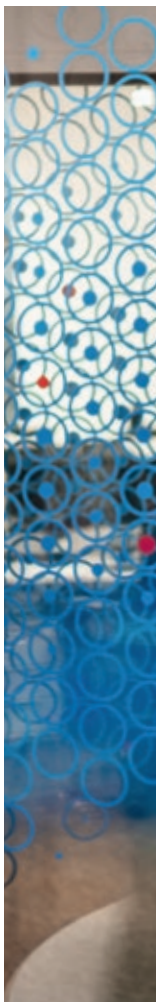
My personal competence lies in coordinating the work of our teams to deliver projects on time. We try to reduce the complexity by releasing as often as possible, measuring the results and taking further action. The applications we create must be customer-oriented and just as easy to use as Netflix or an iPhone.

Last year we launched a new web shop for Japan, and right now we're preparing the complete integration of the China web shop, so customers will be able to order and pay via WeChat, for example.

I'm excited about these new technologies and ideas. However, our task has long since gone well beyond traditional e-commerce. We no longer think in terms of digitalization for individual areas – we want to make QIAGEN a real digital company.

MY STANDARDS

I mediate between business and IT. I have to understand the various needs of people to later turn them into working software solutions. We follow very clear questions: What do you want to achieve? How soon do you need a solution? We also don't wait for someone to come to us; we seek out opportunities to make a difference. It's always about doing a bit more than expected, thinking beyond IT, to question the existing processes, to say, "Let's challenge the status quo!"



Katarzyna Haneczko, Accounts Payable Manager – Employee no. 1

I was hired in November 2012, a month before my current boss. During my interview they said it would be a small company, maximum 100 people, a family atmosphere. Today, there are nearly 500 of us – and yet it still feels like a family.

I started out as a simple accountant, and now I'm the manager of a team of 20 people. My focus is on standardization and automation. What I like about my work is that I can realize my ideas. QIAGEN expressly motivates us to do so. They've told us from day one that we should not only make it cheaper but, above all, make it better.

QIAGEN is an atypical Service Center. We really feel a part of the company, not just a service provider. We know the people in other branches and they know us. We cooperate globally, so wherever you are – whether in Poland, Germany, the U.S. or China, you name it – everywhere you experience the same QIAGEN spirit.

MY GREATEST SUCCESS

One of my most recent projects was the development of a scanning system for all incoming invoices. Previously, this was done by a service provider, but it was expensive, so I wondered if we could do it in-house. I was learning about scanning technologies and processes and so now we've since successfully installed a system that can work with all types of invoices from all over the world. Even the act of sending invoices is automated – hardly anyone here physically touches an invoice anymore. As you can see, we're always looking at what else we can optimize, and where. We motivate our employees to deliver new ideas.

Kaśka

GOING EAST

QIAGEN Business Services (QBS) opened in 2018, in Manila.

Because of the good experiences with the Shared Service Center in Wroclaw, QIAGEN opened a second office of this kind in Manila, in 2018. Like Wroclaw, the Philippine capital is a prime location for a shared Service Center because of its highly educated employee base and good infrastructure. QBS Manila will provide services related to supply chain management and customer care and accounting, as well as technical services and other sales support services, specifically to the QIAGEN businesses in the U.S. and the APAC region. The total headcount should reach an estimated 200 by 2020. The Wroclaw team supported the establishment of the new organization for many months, with its experts working onsite in Manila.

PRODUCT CATEGORIES

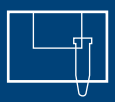
share of 2018 net sales

12%

Instruments

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

88%

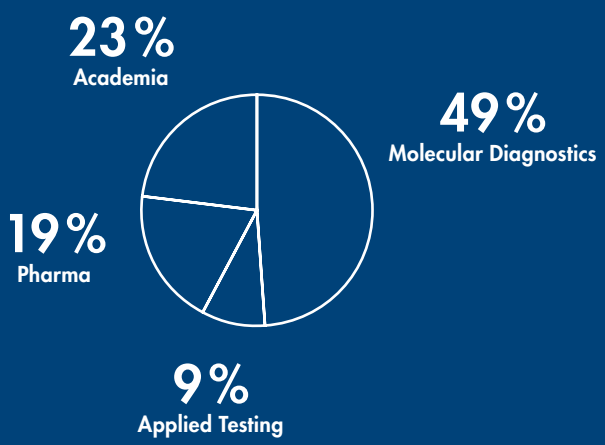


Consumables and related products

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.

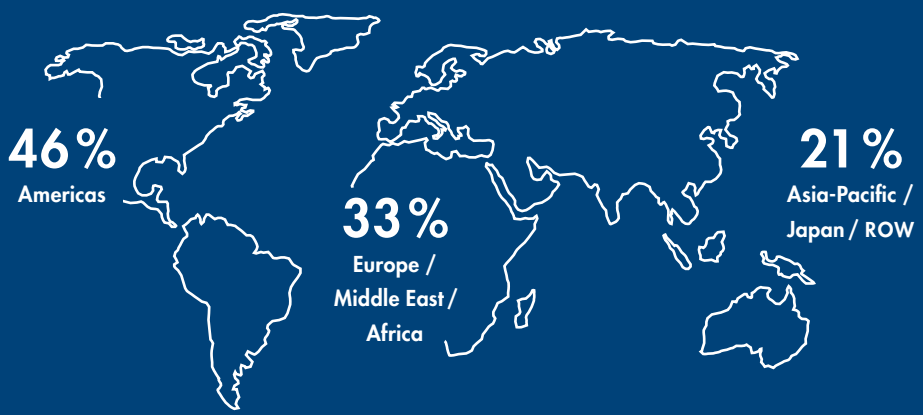
CUSTOMER CLASSES

share of 2018 net sales



GLOBAL PRESENCE

of total QIAGEN Sales



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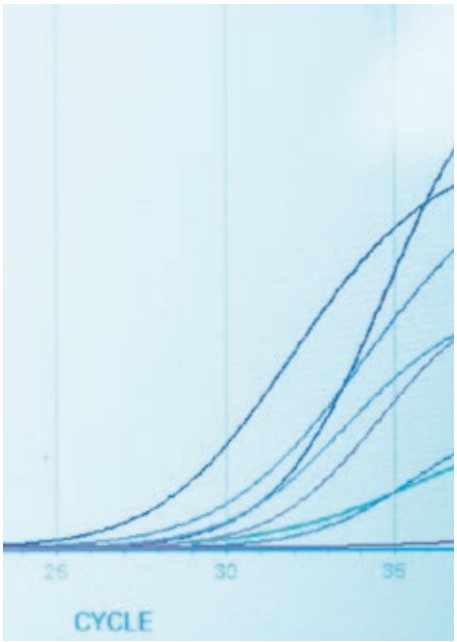
In this annual report QIAGEN uses the term molecular diagnostics. The use of this term is in reference to certain countries, such as the United States, limited to products subject to regulatory requirements.

As of February 2019, QIAGEN molecular diagnostics products included 20 FDA (PMA-approved or 510(k)-cleared) products, 17 clinical sample concentrator products (14 kits and 3 instruments), 69 EU CE IVD assays, 16 EU CE IVD sample preparation products, 18 EU CE IVD instruments for sample purification or detection, 31 China CFDA IVD assays/sample preparations and 13 China CFDA IVD instruments.

This annual report may also contain trade names or trademarks of companies other than QIAGEN.

page 20: QIAstat-Dx will be available in 2019. Product is currently marketed under the name DiagCORE and not available in all countries.

This document contains detailed financial information about QIAGEN 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. QIAGEN also publishes an annual report under IFRS accounting standards, which is available on our website at www.QIAGEN.com.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