



Genetic testing for any species, any organisms, any genes™

Business Summary

PixelBiotech GmbH is a German startup building AI (Artificial Intelligence) powered single-molecule genetic testing technologies and platforms. Being the inventor of the industry's first true multiplex single molecule Fluorescence *in situ* Hybridization (smFISH) probe and an AI-powered data analysis platform, our mission is democratizing genetic testing by making it accurate, universal, affordable and accessible. PixelBiotech's platform technologies will empower our customers to detect any gene from any organism or species at single-molecule single-cell precision.

PixelBiotech is founded in 2018 by Dr. Cheng and Dr. Lou as a spinoff from the Germany Cancer Research Center (DKFZ) in Heidelberg. Our current product line includes the HuluFISH, the true multiplex smFISH, and the HuluREAD, the first industrial AI image analysis software for smFISH data. Since the launch of these two products at later 2018, we have served more than 30 customers from academics and industry in 9 countries. Pilot sales revenue has accumulated to over €94,000 and more than 200 products has been shipped to our customers. HuluREAD has successfully analyzed more than 1 TB image data from our customers.

To make a meaningful breakthrough in the market of genetic testing, PixelBiotech is developing a hardware device, HuluSCOPE, which will enable hospitals and doctors to receive test results for diagnosis at the point-of-care, i.e. within a very short time frame, and at affordable cost (Figure 1). The prototype development and the clinical validation of a COVID-19 rapid testing kit on HuluSCOPE are estimated to cost €100,000 per month over the next 36 months. We have signed a seed funding with BW Startup BW PreSeed program with €400,000 convertible loan. We are also in application of several public funding in Germany and Europe in response to COVID-19. One of the largest funding would be the EIC Accelerator SME Instrument with €2,500,000 budget. Additional funding from public and private sectors will dramatically speed up our development in HuluSCOPE prototype and COVID-19 rapid test kit's clinical approval.



Figure 1 HuluSCOPE Concept for Automated Genetic Analysis of Single Molecule/Single Cell

Customer Requirements Currently Underserved

Many important healthcare or related industries are underserved by today's genetic technologies like Next-Generation Sequencing (NGS) or Polymerase Chain Reaction (PCR) (Figure 2). For genetic testing purpose, the existing technologies do not satisfy the customer needs in terms of performance, precision and price.

NGS has intrinsic characteristics of high instrument set-up and consumable cost, low accuracy introduced by library amplification bias, and poor portability in hardware design. It has been successfully deployed in many research labs to provide powerful discovery of genomic scale information for many

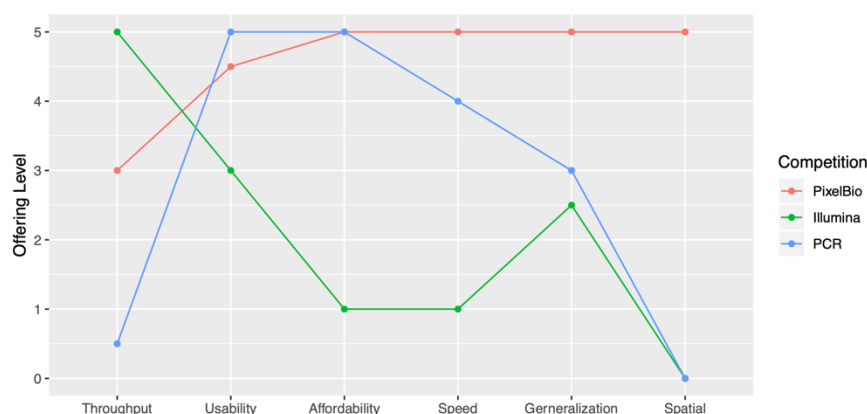


Figure 2 Competition Analysis with NGS and PCR Based Genetic Testing

biological problems. It has also been adopted in certain genetic testing of mutation panel for cancer patients to identify the right treatment for specific subtype patients. However, it has not become the working horse for genetic testing. Cost and turn-around-time (TAT) is a major drawback since one test will still cost around \$1,000 or more. Not to mention the prediction power generated from a large scale correlational study of genomic data without a proper understanding of the disease mechanics.

PCR based assays are still the current working horse for the genetic testing (or molecular diagnosis). But they are still limited by their low throughput set by the readout mechanism in a PCR machine or high false-positive rate due to extensive rounds of exponential amplification. All PCR machines could only read one target per fluorophore used in the assay. If one fluorophore is used as a reference, the total target number is limited to maximally 4. Automation of PCR, combining with microarray-based hybridization detection, the target number of PCR can go up to 20 species, but with the trade-off in speed due to additional hybridization and detection steps. For example, the Bosch's Vivalytic and GeneMark Dx's eSensor requires 4-6 hours to complete.

The quantification result of real-time PCR is a regression result from the log-linear relationship between the PCR cycle number and the relative quantity of input analytes. This regression result is inherently sensitive to PCR amplification bias caused by the buffer recipe, the target sequence, and primer selection, etc. No matter how successful the PCR may currently be, its nature will restrict its potential in modern genetic testing applications. A modern genetic testing would have to be both high-throughput (up to hundreds of targets in one assay), low-cost (to allow user equality for all humankind), and portable (for deployment in all areas and environments).

The technical limitations of the currently available technologies prevent the community to respond quickly to a large number of applications where speed, cost and throughput are all required. For example, in food safety, the outbreak of African swine fever virus (ASFV) has cost \$300M+ loss to the Chinese pig farmers in 2018 and world protein production has been reduced by half in 2018. Now it has affected 25 countries and areas in the whole world. Due to the notoriously long half-life (months) of the ASFV, it is estimated that the eradication needs at least 5 years. The first incidence of ASFV in China is several months before the outbreak. This is the same scenario with other outbreaks like the Ebola outbreak in 2016 and the COVID-19 started in the end of 2019. The SARS-CoV-2 outbreak has already caused \$18 trillion loss in the world stock market and expected \$1.1 trillion loss to our world's GDP in 2020. On March 11th, the WHO officially has declared COVID-19 a pandemic. By April 5th, over 1,203,000 cases of have been reported (many more are still unreported) and have already led to over 64,795 confirmed deaths (Figure 3).

The reasons for these outbreaks are always complex with cultural, political and technical reasons entangled together. But the technical simplicity and agility of a global pathogen surveillance networkd would have reduced the hurdle for stakeholders in different industries. This network would have been helping us to actively monitor the pathogen burst and control the spread of infectious disease for human or animal health. Interviewing with several stakeholders in animal infectious disease control, we have concluded 10-20% percent of the economic value of the pig is a reasonable price range for pig farmers to pay for a life-cycle active pathogen surveillance for up to 30+ viral/bacterial infection. For human infectious diseases, it would be great if we could screen each suspected cases, if not the whole population.

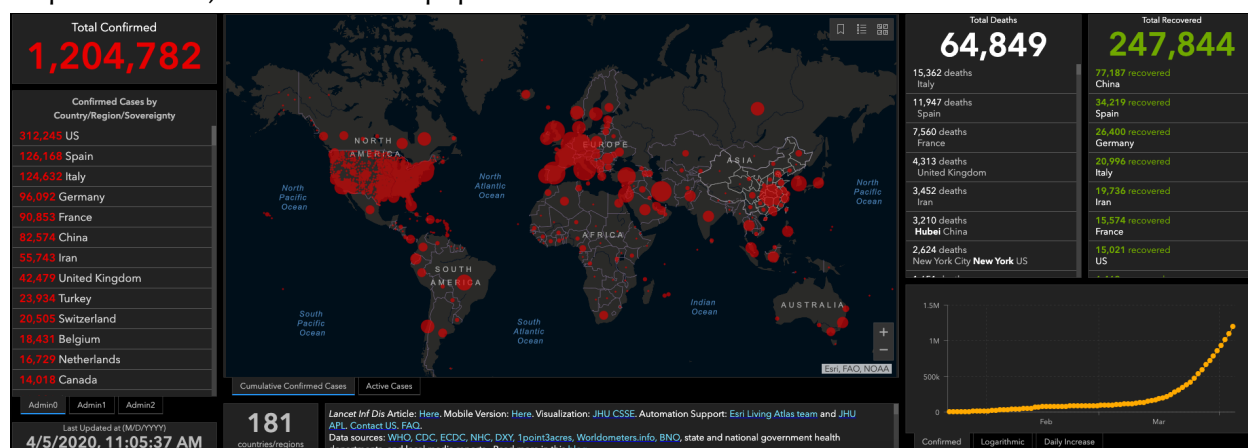


Figure 3 Global Pandemic Map of COVID-19. Source: Coronavirus Resource Center, JHU.

In the vaccine industry, recent accidents and lawsuits (i.e. Changsheng Biotechnologies Ltd's falsified documentation of vaccine quality control) have also raised the need for affordable and high throughput vaccine quality control tools over 20 virus contamination for biological products. A low-cost yet high-throughput tool for controlling the potential virus contamination in vaccine production, vaccine dosage determination will also allow vaccine company to apply active quality control in China.

In the cell and gene therapy, a low-cost, precise solution for continuous molecular profiling and outcome monitoring is still missing. For example, in the latest achievement of the CAR T-cell therapy (Chimeric Antigen Receptor, an engineered human T cell for killing tumor cell), there is still no effective measurement to visualize the CAR positive T cell after infusion in the patient, especially for the broader application of CAR T cell in solid tumors. This prevents pharma industry to continue the miracle of this half million-dollar blockbuster drug in fighting against more cancer types and reducing drug-resistant rate.

The world is connected than never before. In current globalization movement, especially the rising economic importance of Asia, pandemic like COVID-19 is inevitable due to the deeper connected economy and people. One virus outbreak can potentially reach any location in the world within 36 hours. Any outbreak in animal kingdom or human society will initiate a butterfly effect in the world economy and our healthcare system. The issue raised from the globalization should not stop the globalization, given the fact so many benefits delivered by the globalization. It simply means our globalization process must move to new development stage where we need tight, coherent and efficient management systems for various global issues, including the pandemic surveillance. Globalization is not the problem, managing the globalization is the real problem.

Pandemic and other healthcare problems need a global management.

Neither hope nor avoiding is the best strategy.

PixelBiotech Technology

PixelBiotech offers the performance and precision required by genetic testing at affordable prices by combining a new technology with AI.

We are leading the industry in developing highly generic, very affordable, multiplexing smFISH probes. Our proprietary smFISH technology HuluFISH provides precise gene expression profiling at a single molecule level up to 120 targets with entry-level fluorescence microscope with 4 lasers. The HuluFISH has been exclusively licensed from DKFZ for its global commercialization by PixelBiotech. The HuluFISH is the first industrial enzymatic FISH probe labelling technology with multiple fluorophores (Figure 4). With this labelling technology, our probe could have a combinatorial barcoding for multiple targets in one reaction. This barcoding mechanism overcomes the readout limit in PCR. HuluFISH detects $C(n*(n+1)/2, 3)$ targets with just n fluorophores. This brings the throughput to fulfill the requirement in mutation panel detection for cancer, which is usually detected by the high cost NGS technology.

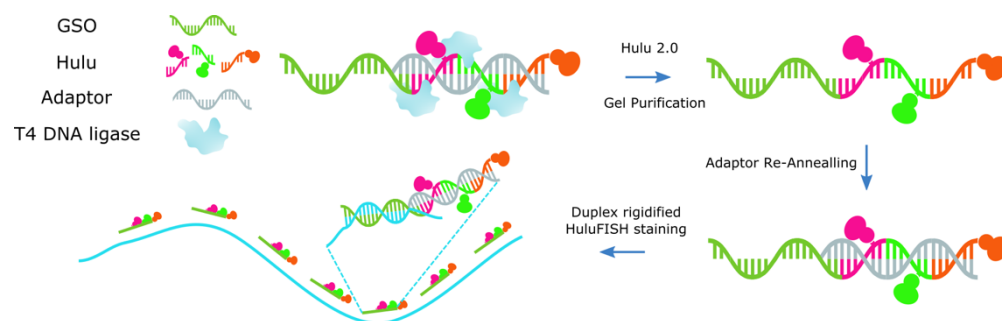


Figure 4 Industry's first true multiplex single molecule Fluorescence In Situ Hybridization (FISH) method, making it possible to detect pathogens with a single molecule sensitivity.

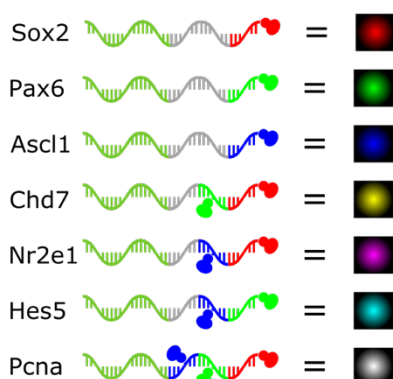


Figure 5 Successful deconvolution of 7 genes in mouse embryonic brain using our proprietary HuluFISH.

We have also developed the HuluREAD – a comprehensive AI-powered data analysis platform that is 3000x faster than humans, effectively eliminating the gap between data and discovery. The core of the HuluREAD is built on state-of-the-art deep neural networks (DNN) based 3D object detection and segmentation algorithms, including FISH spots, nuclei and cells. Different models have been developed to support various experimental setups and imaging conditions. The HuluREAD also features advanced image processing algorithms such as adaptive intensity correction, automated outlier detection, automated noise estimation and robust FISH spot shape fitting. The output of HuluREAD is a single Excel spreadsheet file that contains all the information useful for users. Many preliminary and advanced statistics are included therein such as count, size,

HuluREAD
AI-POWERED IMAGING DATA QUANTITATION, COMPLETELY FREE.

- > **SCIENTIFIC**
Designed by scientists.
Developed for scientists.
- > **FAST AND ACCURATE**
Built on state-of-the-art deep learning and image analysis.
- > **QUANTITATIVE**
Abundant imagery features and statistical analysis
- > **PUBLICATION READY**
All you need to know about your data in a single report.
- > **BRAIN-DEAD SIMPLE**
No installation, no tuning.
Calling service in seconds.
- > **HIGHLY ACCESSIBLE**
Fully cloud and web based.
Service accessible from anywhere.

intensity, mRNA quantitation, nearest neighbor distance, cross-channel encoding, etc. The HuluREAD has been used to analyze data generated from various microscopes (Zeiss, Dragonfly, Nikon, Leica) and species (microorganism, mouse, human). The HuluREAD brings high efficiency and standardization, and is a key element in improving the usability of our HuluFISH technology.

From our current customer feedback, the most wanted feature from PixelBiotech is a dedicated fluorescence microscope for HuluFISH experiment. Therefore, we have started the design of HuluSCOPE from 2019 for ASFV single molecule on-chip detection. The global spread of COVID-19 necessitates our HuluSCOPE development toward human health care. In the following 36 months, **we will bring the HuluSCOPE – a diagnostic Point of Care device able to identify any pathogen of interest in 15 min – to market readiness.**

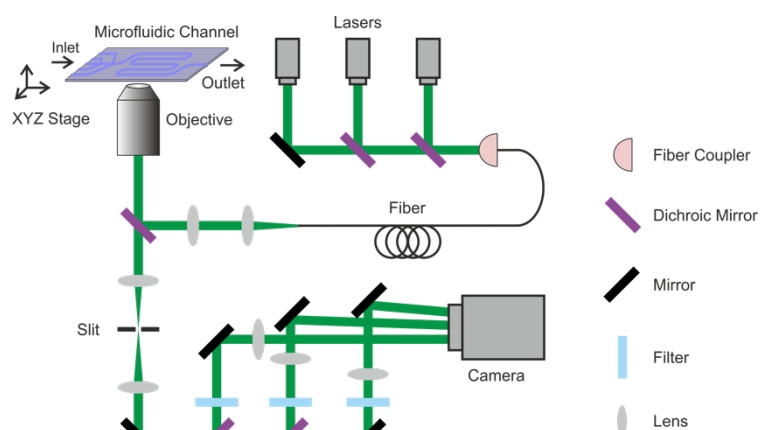


Figure 6 HuluSCOPE Optic and Microfluidic Design with 3 Channels.

HuluFISH can be used both for *in situ* tissue/cell sample or nucleic acid in solution. Traditionally FISH technology is used for detecting gene expression *in situ*. HuluFISH has been successfully tested from our customers on variety of tissue/cell samples from yeast to human. On the other hand, HuluFISH detection for isolated RNA/DNA biomarkers in solution has also been realized by the HuluFISH-on-Chip design. The HuluFISH-on-Chip setup requires only standard fluorescence microscope with way less background staining noise and much easier hardware setup. Therefore, its technical simplicity allows us to develop the HuluSCOPE with a simple configuration tailored for HuluFISH-on-Chip experiments (Figure 6). Ultimately, the HuluSCOPE will further evolve into an automated microscope with microfluidics control for easy RNA/DNA isolation and loading on to a glass chip surface for HuluFISH staining and single molecule counting. As a result, the HuluSCOPE will provide a test that is 1000x cheaper and 200x faster than NGS, 20x faster and 40x cheaper than PCR.

HuluSCOPE uses our AI-powered algorithm HuluREAD and patented HuluFISH technology to automatically process and analyse samples on a microfluidic chip. With the broad deployment of this device, we are able to build a surveillance network with real-time monitoring of all dangerous pathogens and prevent these diseases from becoming the next pandemic. The HuluSCOPE will be sold or licenced to clinics and hospitals where complete detection of up to 120 varieties of virus/bacteria/parasite infections can be finished within 15 min on the spot. Patients can be hospitalised or quarantined immediately, if required. **One test will cost only €1 to payers, making mass-testing perfectly feasible regardless of whether payers are healthcare systems, insurance companies or individual patients.**

HuluSCOPE is the perfect all-in-one system for developing rapid diagnosis for COVID-19 pandemic and ASFV epidemic. To validate the HuluFISH's capability in counting individual molecule of virus sequence on a chip, we use synthetic ASFV DNA to simulate the extracted nucleic acid from ASFV containing biosample. A consensus probe set for all variants of p72 gene in ASFV has been designed to visualize ASFV synthetic DNA on chip. Serial dilution of ASFV from 10^9 to 10^5 copies/ul has been tested with manual droplet-based hybridization on a glass surface, and detected with a commercially available microscope. Current set up has achieved 10^5 copies/ul.

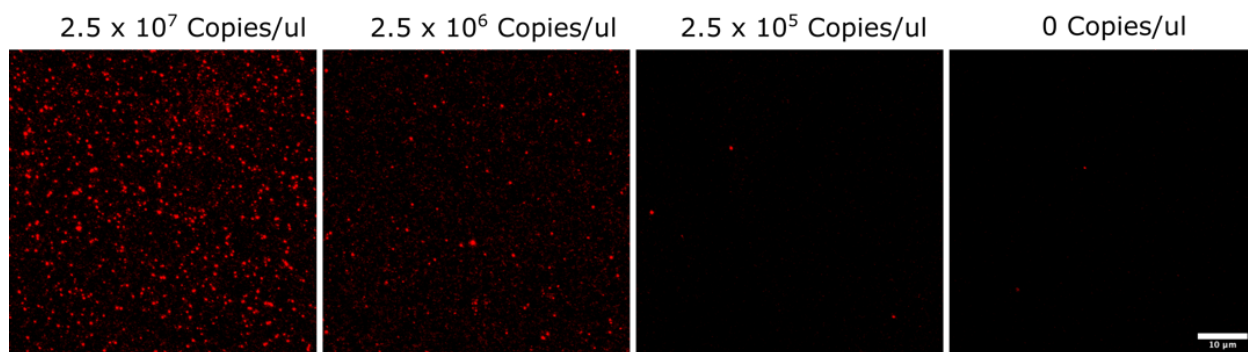


Figure 7 Single molecule counting of ASFV DNA. Concentration dependence counts for ASFV is shown from left to right, $1E7$, $1E6$, $1E5$, 0 copies/ul.

There are several modifications can be applied to improve the sensitivity up to 1 copy/ul. These improvements are enrichment of nucleic acid before hybridization, larger sample input, microfluidic facilitated efficient hybridization, and coating chemistry to reduce any non-specific binding.

- 1) Enrichment will be done with sequence specific capture oligonucleotide probes, typically allowing for 50+ fold enrichment.
- 2) Current RT-PCR method for SARS-CoV-2 only use 1/20 of the purified RNA for PCR reverse-transcription and amplification. HuluSCOPE will use all virus RNA molecules in the biopsy samples and have a 20-fold increase in input molecules.
- 3) We have only imaged $50 \times 50 \mu\text{m}^2$ on the glass slide. The final HuluSCOPE will have a $200 \times 1000 \mu\text{m}^2$ flow channel for imaging. This will further increase the dynamic range of detection, as well as the detection limit.
- 4) Higher hydrophilic surface coating with polymers or modification in hybridization solution will dramatically reduce the non-specific binding we see in the zero control (water, Figure 7). Additionally, the microfluidic reaction chamber for single sample will also exclude the possibility of cross-contamination generated specific binding in zero control from positive samples. With the reduction in non-specific binding and increase in scanning area in 3), the limit of detection can be further increased by a factor of 80.

In total, the incorporation of microfluidics in HuluSCOPE can enhance the sensitivity of limit at least by a factor of $20 \times 50 \times 80$ (0.8×10^5). In agreement with our estimation, Nilsson's lab has demonstrated a direct single molecule counting of rolling circle amplified nucleic acid target on glass surface at the sensitivity of 1 copy/ul (1.2 aM, Figure 8). We will develop the microfluidic cassette for automated detection of pathogen nucleic acid. A microfluidic detection chamber will allow us to automate the entire detection process, from nucleic acid extraction to image acquisition. The $50 \mu\text{m}$ height of the detection channel in the microfluidic cassette will speed up and increase the efficiency of hybridization reaction. Automated nucleic acid extraction and enrichment from nasal swab will be incorporated into

the cassette. With the rapid and efficient hybridization inside a microfluidic chamber, we expect to reach our targeted 1 copy/ul detection sensitivity.

	Dynamic range	Sensitivity (concentration)	Multiplexing capability	Cost/ Required instrumentation
RCP enrichment	5 logs	1.2 aM	5-plex*	Low/standard fluorescent microscope
Digital PCR (BioRAD)	5 logs	1.6 aM (37,38)	2-plex	High/three instruments for droplet generation, PCR and droplet read-out
Nanostring	6 logs	100 aM (6)	800-plex	High/two instruments for sample preparation and digital analyzer
NGS	4-6 logs depending on library prep. and seq depth	~0.5–30% molecule detection efficiency depending on library prep. and seq depth (9,39,40)	Not limited	High/diverse sample prep. equipment, complex library prep. schemes and expensive NGS reagents and instrument

Figure 8 Comparison of Current Digital NA Quantification Methods. Source: doi: 10.1093/nar/gkw1324.

HuluSCOPE is also extensible for other disease areas. The microfluidic cassette for pathogen detection can be readily modified for single cell diagnosis, where intact cells will be directly captured, stained and imaged for rapid diagnosis. To demonstrate with a proof-of-principle experiment, we have been collaborating with Prof. Dirk Jäger at NCT Heidelberg on single cell characterization of CAR-T cell for manufacturing quality control and after-transplantation prognosis monitoring. We have preliminarily shown that CD3 and CAR mRNA co-expression can be visualized and analyzed at single molecule/single cell level (Figure 9). Most of the CAR engineered human T cells have co-staining of CD3 (Red) and CAR (Green), while matched control donor T cells only have CD3 staining. The experiment demonstrates the specificity of HuluFISH on CAR single molecule counting in situ, as well as the power of image-based single cell quantification and quality distribution.

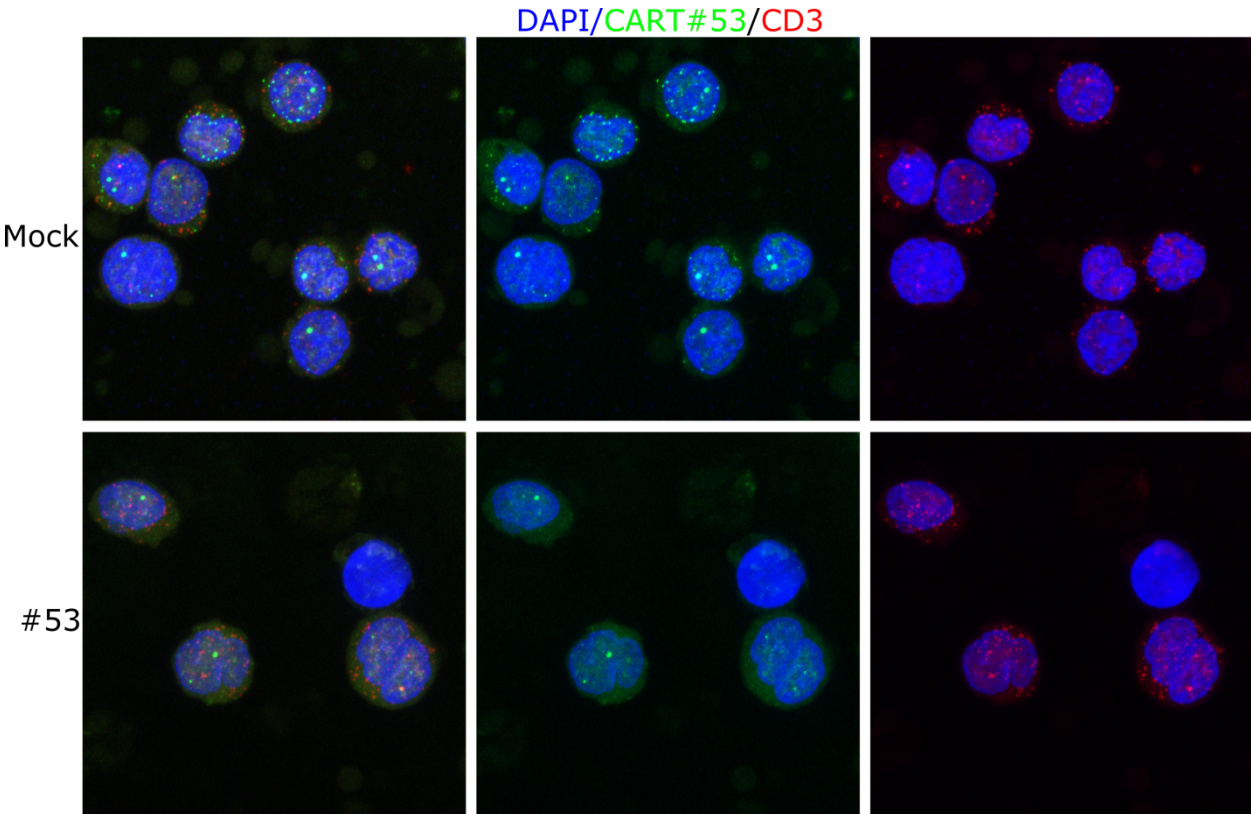


Figure 9 Single Molecule Counting In Situ for CD3 and CAR in Human T cells.

In the future, more biomarkers up to 120 genes can be included in the single cell quality control and prognosis of CAR-T. This study is indicating other gene therapy products could be evaluated as CAR-T cells for higher efficacy and safety. Additionally, **early cancer diagnosis** based on circulating tumor cells or tumor DNA/RNA could also be analyzed with HuluSCOPE and developing into a rapid, cost-effective, data-rich diagnosis for populational level screening efforts.

Products and Services

Since later 2018, we have successfully launched 3 different products and services: HuluFISH, HuluREAD and HuluONE. In our pilot sales period, we have served more than 30 customers from 9 countries and 5 different industries.

As illustrated by our product and service roadmap (Figure 10), we will be working on new innovations in order to deliver the HuluFISH and the HuluREAD technologies to a broader base of customers with products offering easier and simplified user experience. It will be enabled by our commitment to the long-term development of a fully automated device with minimal hands-on time for end users. The next important product on our road to innovation is the HuluSCOPE.

Following is a brief description of all products shown in the roadmap (Figure 10).

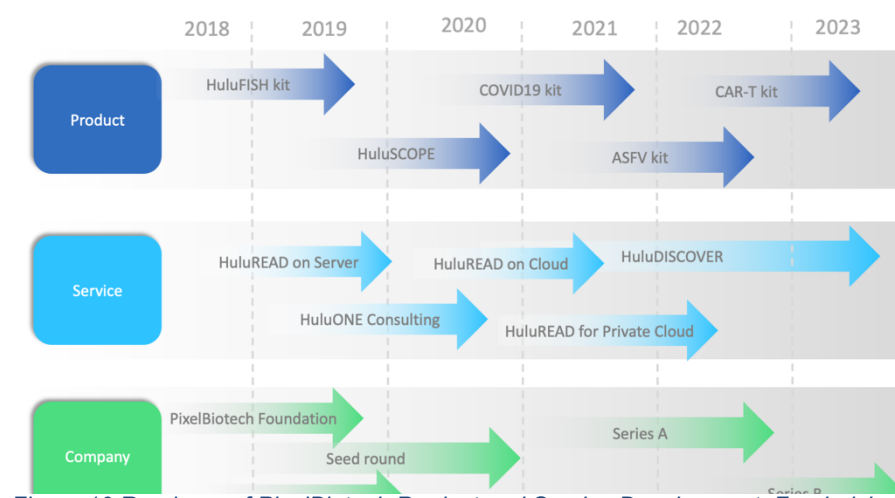


Figure 10 Roadmap of PixelBiotech Product and Service Development, Fundraising.

- 1) The HuluFISH Kit is the industry's first true multiplexing smFISH probe kit that detects multiple biomarkers in a single hybridization reaction. Our probe design is programmatic, allowing for full customization of combinations of genes. We only need the sequence or database id of targets from our customer.
- 2) The HuluREAD is an AI-powered cloud platform for HuluFISH data analysis. HuluREAD features deep learning, 2D/3D image segmentation, quantitative feature extraction, statistical analysis and automated reporting. The HuluREAD provides a high level of quantitative standardization and removes tens of hours of manual labor per experiment.
- 3) The HuluONE is our lab consulting service for deploying HuluFISH in various vertical applications. This consulting service is helping customers who are not expert in FISH experiment. The service content includes experiment framework design, application specific probe design, sample pretreatment optimization for HuluFISH, imaging acquisition optimization, etc. The idea of this service is having frictionless adoption of HuluFISH in

customers' application. The HuluONE can also be the basis for our CRO (Contract Research Organization) service for both academic and industrial customers.

- 4) The HuluSCOPE will be our third pillar product exclusively made for HuluFISH imaging. This microscope is a fluorescence microscope with 4 lasers for imaging 120 targets in a single experiment. HuluSCOPE 1.0 will only work for HuluFISH-on-Chip experiment. And the HuluSCOPE 2.0 will be equipped with new functionality to scan HuluFISH in situ experiment as well. The HuluSCOPE 3.0 will be the ultimate version of the HuluSCOPE with fully automated sample preparation, loading, HuluFISH staining, and imaging. The HuluREAD will also be available on HuluSCOPE for real-time image analysis. HuluSCOPE will firstly serve customers from clinical and animal health, help them to quickly diagnose infectious pathogens. It is a compact HuluFISH device can be installed either bedside or a pig factory farm for active monitoring of infectious diseases. The internet connectivity of HuluSCOPE will also allow our customers to build an **internet of pathogens**, a real time monitoring network for all dangerous microorganisms.
- 5) The HuluDISCOVER is the data/knowledge sharing and technology transfer platform for HuluFISH customers and mid-party service providers. Especially with HuluSCOPE, HuluFISH service providers can develop more vertical applications like we are internally developing for CAR T kit and ASFV kit. The HuluDISCOVER will also include finance investing program for service providers to facilitate the commercialization of their HuluFISH products for specific end customers.
- 6) The CAR-T kit is currently under development and it will be the world's first single molecule single cell gene expression profiling kit for CAR-T cells. It can help pharma industries to have detailed characterization of the quality of the engineered T cell population. For example, how CAR gene is expressed at single cell level and what is the distribution of T cell subtypes. For CAR T treated patient care, CAR T kit will be the most sensitive prognosis tool to monitor the engineered T cell inside the body for a long period.
- 7) The ASFV kit is a comprehensive panel of infectious disease diagnosis kit. It will cover 30+ dangerous pathogens for pig, including ASFV. This kit will be the first kit based on HuluFISH-on-Chip. The proof-of-principle experiment has successfully shown the promise to detect single virus copy on a chip.
- 8) The COVID-19 kit will be a panel of 30 the most common pathogens causing pneumonia. These will include strains of the coronavirus (SARS-CoV-2 included), influenza, as well as bacteria such as *Streptococcus pneumoniae*. The 20 customized HuluFISH probes will be sold as a COVID-19 kit for swift identification of pneumonia causing pathogens at the Point of Care.

Target Markets

We tackle the \$20 billion global genetic testing market with three initial targets. First, we are developing a single molecule level diagnosis and prognosis tool for cell and gene therapies. This market is a rapidly growing market with 21.9% annual increase and \$6 billion market size at 2017 (source: [Coherent Market Research](#)). Our pilot data with CAR-T cell has shown industry's first successful detection of CAR gene expression in human T cells at single molecule precision. Second, we are

developing a universal and high-throughput pathogen detection platform for food safety. The first use case is ASFV detection for the China market (1.12 billion pigs consumed annually). Third, we continue supporting academic and corporate single molecule and single cell research for revenue generation, application discovery and branding.

With the focus on these initial markets, we are going to continuously evolve our HuluFISH platform for broader market penetration, especially the development of HuluSCOPE. The CAR-T and ASFV project will be the playground for our product line to thrive. Both products will start from an elementary version bundled with third party microscope to the ultimate version exclusively working on a HuluSCOPE. Initially centralized service provider will help us to analyze hundreds of thousands of samples from end users based on the elementary version. Later on, the HuluSCOPE powered CAR-T COVID-19 kit and ASFV kit will let more end users like hospitals, pharma companies and pig factory farms to get on-site detection quickly and easily. On the other hand, the academic market will help us to experiment new killer applications like we have found with CAR-T and ASFV.

During the maturation of our product line, there are several additional market opportunities will be interesting to us as well. These are foodborne illness, vaccine safety, animal/human infectious disease control, prenatal screening, drug discovery screening, early and precise cancer diagnosis. Foodborne illness, vaccine safety, animal/human infectious disease control, and prenatal screening will share the same technical foundation we would have developed for ASFV. These are just expanded panels for a HuluFISH-on-Chip assay on a HuluSCOPE. Drug screening and cancer diagnosis will be empowered by the development experience with the CAR-T kit. Harnessing the single cell and single molecule precision, drug screening and cancer diagnosis will be upgraded with new generation of rich data with dozens or even hundreds of gene expression with spatial information included. This new type of diagnosis data will help clinicians to develop a more precise and reliable assay.

Customers

During the presale we have reached €94,000 sales from 30+ paying customers. Our customer base shows diverse regions (Germany, the US, China, etc.) and applications (cell biology, biochemistry, single cell genomics, cell therapy, cancer biology, microbiology, etc.). The HuluREAD has processed terabytes of customer data acquired from a variety of microscopes incl. Zeiss, Leica, Nikon, Andor Instrument, etc. With the continuous maturation of our sales channels and the HuluREAD on Cloud, more individual researcher will have better access to our products and services.

Additionally, the HuluONE will help us to attract more industrial customers interested in single molecule genetic testing service. The ASFV development is the first successful example of the HuluONE service. The motivation for the ASFV kit development is coming from the customized service of detecting ASFV with HuluFISH probe.

With the maturation of HuluSCOPE, our customer base will expand into more categories. Some of these are listed here: 1) clinicians for fast pathogen diagnosis. 2) animal product provider for broad

pathogen active control. 3) food industry for active monitoring of antibiotic resistance bacteria like *E. coli*, *Salmonella enterica*, etc. 4) vaccine companies for contamination control in vaccine. 5) stem cell therapy pharma companies for virus contamination control or other quality control at single cell precision. As a fundamental technology to detect DNA/RNA, HuluFISH is able to replace current genetic technologies to deliver a fast, cost-effective yet high throughput diagnosis based on genetic information.

Business Model

We are transforming the single molecule and single cell industry into a product-service hybrid business. PixelBiotech will be platform company with revenues from direct sales of device and consumables, as well as service fee and royalty fee from our partners. For academic and corporate research, we sell customized HuluFISH probes bundled with the HuluREAD at half the price of competitors, yielding a 70%+ margin. For clinical and industrial applications, we develop and deploy end-to-end testing services with a target 50%+ margin at a much larger volume. To achieve this business expansion goal, we need the following strategy to ensure our products and services reach a broad spectrum of customers offering them a frictionless experience of HuluFISH experiment.

Business support model

- 1) *Setting up the HuluFISH Community Master (HCM)*. In each institution or city, we find one senior PhD student, postdoc, or scientist who is familiar with HuluFISH technology, or having some experience with the RNA staining, RNA quality management, or related troubleshooting. The HCM will serve as a facilitator for HuluFISH sales in their area. They are motivated by sales commission in the form of valued gifts or internet money, due to the contract issue in Germany. Their tasks including organizing workshops, lectures about HuluFISH (more broadly spatial transcriptomics, or RNA biology in general), finding new customers, and technically supporting the local HuluFISH user community (the troubleshooting for example).
- 2) *Building scientist oriented elite sales team*. In the following 2-3 years, PixelBiotech intends to merge sales and technical support functions into one job description. The sales team is divided by territory and oversee the HCM in their responsible territory. The sales team should check twitter before they meet customers. The ideas are for a salesperson to know news and science quite well to warm up talks with clients. According to the report, 60% conversational content with customers is not about the products, customer's need. Sales should know how HuluFISH works and become effective at troubleshooting.
- 3) *Establishing a master level marketing team*. The marketing team is responsible for online marketing and training of HCMs. The marketing team should also help to find lead online, like all single-cell customers on LinkedIn (13K+), all single-cell genomics or RNA related paper authors from NCBI (web scraper for author info at PubMed). WeChat and WhatsApp group for PixelBiotech/HuluFISH should also be managed by the marketing team to connect with customers at zero distance. The marketing team should also produce webinars and video tutorials for HuluFISH experiments and applications. Regular updates from our social media

portals like LinkedIn, Twitter, Facebook, WeChat, the official website of PixelBiotech will also be performed by the marketing team.

Business expansion model

- 1) *Distributor*. Sales via a distributor are very critical in several aspects: a) no accounting issue with sales. Sometimes the payment could delay for months after-sales. b) creating vibrant marketing from multiple distributors. Each distributor should be complementary in their established customer sectors. c) no exclusive distributor. All distributors get a different discount based on their sales revenue. The golden distributor has 30% discount up to €20,000. The platinum distributor has 35% up to €50,000. The diamond distributor has 40% discount up to €200,000.
- 2) *Collaborative partner*. Partners are all involved in the specific vertical application for HuluFISH, such as ASFV and CART. With Partners, PixelBiotech will negotiate a case-dependent collaboration agreement covering sales split percentage. Initial revenue from partners is the development fund to kick off a specific project. Once the project survived in the prototype phase, product development would be co-financed by PixelBiotech and its partners and future sales mostly will come through a partner company.

Competition

Our main competitors are mainstream genetic testing technology companies (Figure 11). PixelBiotech has a unique combination of advantages in throughput, cost, runtime and sensitivity.

NGS generates omic-level genetic data yet is very expensive. Its powerful discovery capability makes it ideal for research purposes, but too costly in design to be developed as routine diagnosis tool. Immunostaining and PCR are more cost-effective than NGS but can only detect at most a dozen of biomarkers in a single reaction. This limits the broad usage of these techniques in new emerging threats from infectious disease control, precise and personalized diagnosis of complex diseases like cancer. The HuluFISH combines the strengths from both categories, becomes very low cost in routine diagnosis while maintaining the high throughput for big data driven prediction.

Company	Illumina, Nanopore, Thermo-Fisher, etc.	Thermo-Fisher, Bio-Rad, Qiagen, etc.	Abcam, R&D systems, etc.	PixelBiotech GmbH
Technology	NGS	PCR	IHC	HuluFISH (smFISH)
Amplification Bias or Sample Cross-over Contamination	High (require PCR)	High	None	None
Detectable Market Types	RNA/DNA	RNA/DNA	Protein	RNA/DNA/Protein
Detected Markers in a Single Reaction	Omic level	1 to 4	1 to 12	1 to 127
Turnaround Time	11 to 28 days	1 day	2 days	10min-1 day
Sensitivity	Pooled detection	Pooled detection	pg to ng/ml	Single molecule single cell level
Spatial Information	No	No	No	Yes
Cost in Practice	High	Medium	Medium	Low

Figure 11 Competing technique comparison for HuluFISH.

Compared with traditional FISH technologies which suffer from very limited throughput and do not offer data quantitation services, the HuluFISH offers the best value for traditional customers in FISH market sector (Figure 12). More importantly, the brand-new production design chemistry of the HuluFISH offer the chance to reduce the probe production cost up to 20x, which allow us to have a superior price model to give our customers the best FISH probe they could have. It is brighter, cheaper and detects way more targets in one reaction. The FREE service of HuluREAD will be another game changer in this field, and bring the competition to a new level. The company who is able to provide unified products and user experience will achieve greater customer satisfaction in the long run.

Company	Abbott	Agilent	ACDBio	Biosearch	PixelBiotech GmbH
Product	Vyiss IntelliFISH	SureFISH	RNAscope	Stellaris	HuluFISH Kit
Technology	BAC clone based DNA FISH	Chip synthesized DNA FISH	smFISH	smFISH	HuluFISH
Detected Markers in a Single Reaction	1	1	1 to 4	1 to 5	1 to 127
Data Quantitation Software	NA, manual counting under microscope	NA, manual counting under microscope	Required purchase 3 rd party software	NA	Custom built and free of charge
Sensitivity	Single DNA molecule	Single DNA molecule	Single RNA molecule	Single RNA molecule	Single RNA/DNA molecule
List Price	€4500	€1587	€1400	€900	€499

Figure 4 Comparison with traditional FISH techniques and vendors.

Competitive Advantages

To compete with existing giants in this industry, we have the following competitive advantages to help us survive and thrive:

- 1) Access to one of the largest cancer biology sample/data banks in the world at DKFZ. This resource will ultimately help us to collaborate with DKFZ researchers to develop more early and precise diagnosis kit for cancer patients.
- 2) Inventor/owner of generic, affordable, multiplexing smFISH probe technology with global IP protection. Having the inventor in the founding team will allow continuous improvement of HuluFISH to have more competitive advantages.
- 3) The only FISH supplier offering free AI-powered data quantitation service. This unique identifier of PixelBiotech will help us to keep customers sticky to our products and services.
- 4) Provide 10x throughput at half the price of the closest competitor. This help us to convince customers to buy 4x more probes than our competitors and even give us more revenue per order.
- 5) Pioneer in a novel biotech/AI hybrid business model. The interdisciplinary gene in PixelBiotech will let us to become the new generation of biotech company with more digitalization.
- 6) Unified platform technology with HuluREAD, HuluFISH and HuluSCOPE serves more customers in various industries.

Founders and Team

- 1) Yong-Sheng Cheng, Co-founder, HuluFISH inventor, 10+ year biotech R&D, 10+ papers incl. Nature.
- 2) Xinghua Lou, Co-founder, 10+ year AI R&D, best paper awardee, 30+ papers incl. Science and MIT Press.
- 3) German Cancer Research Center, Co-founder, top biomedical R&D institute, two nobel laureates in the past 10 years.
- 4) Haisen Ta, 10+ year single molecule microscopy research experience from Nobel Laureate Stefan Hell's Lab, 15+ papers incl. Nature Methods.
- 5) Vipin T Sreedharan, 10+ year bioinformatic research and development.
- 6) Christoph Thiemann, 9-year software development and project management.
- 7) Dr. Sreemukta Acharya, Head of Marketing, 10+ year biomedical research and 3-year social media marketing.
- 8) Odomar Vancraeyenst, CFO, 30+ year in financial industry, expertise in financial risk management and planning.

Advisors

- 1) *Prof. Dr. Dirk Jäger*, Managing and Medical Director of the National Center for Tumor Diseases, Germany, Head of the Medical Oncology Department at the Heidelberg University Medical Center, a world-class researcher in CAR T cell therapy.
- 2) *Dr. Lidai Wang*, Assist. Professor in Hong Kong City U, China, a world-renowned expert in photoacoustic imaging and the inventor of single-cell flowoxigraphy (FOG).
- 3) *Dr. Patrick Schmidt*, Group leader of the National Center for Tumor Diseases (NCT) Heidelberg, improving CAR-T for liquid and solid tumors.