

Conference Report of the 3rd Swiss Symposium in Point-of-Care Diagnostics held online on 29 October 2020

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Abstract: The COVID-19 pandemic has raised in 2020 an unprecedented need for diagnostic testing, especially rapid testing, for SARS-CoV-2 infections. POC diagnostic tools, however, have clearly also importance in other domains such as oncology and women's health, because of the efficiency and convenience factors playing an increasingly important role in a mobile (and sometimes confined) and digitally connected world. Out of necessity, the 3rd edition of the Swiss Symposium in POC Diagnostics, originally planned to take place at the La Poste Conference Center in Visp, was smoothly run *online* with 170 engaged participants from science, industry and laboratory medicine.

Keywords: Blockchain · COVID-19 · CRISPR/Cas · Exhalomics · Lockdown · Patient Empowerment · Preeclampsia · SARS-CoV-2 · SHERLOCK · Telehealth · POC Cell Counts

1. Are POCT Devices Suitable for Medical Diagnosis?

In a time of urgent need for COVID-19 rapid tests and when a plethora of new diagnostic products are brought onto the market, this interrogative title may appear provocative, but indeed is legitimate and important. **PD Dr. Michel Rossier**, Head of the laboratories of the Institut Central des Hôpitaux (ICH) in Sion reminded during his speech that “the physician is central to the diagnostic process”. In addition to lab tests, a doctor takes epidemiological data, patient anamnesis, physical exam and other tests

(e.g. imaging) into account when making a diagnosis. We need to keep in mind that there is always a certain risk of obtaining false positive results, and disease prevalence can heavily worsen this rate. Additionally, POC devices often underperform in terms of precision and may show poor concordance with central lab systems. In the worst case inaccurate results may pose a serious risk to patient safety, particularly when the diagnostic test gives inappropriate guidance to therapy. Inaccurate results may not come necessarily from the measurement process, but may be due to pre-analytical steps, e.g. insufficient manual sample loading by the operator (training issue).

Notwithstanding these limitations, POC diagnostic tests have their role to play, for instance when a large population needs to be screened as in the case of the COVID-19 pandemic. Dr. Rossier mentioned that the ICH performed more than 1600 SARS-CoV-2 RT-PCR tests per week during the spring peak and almost 7000 tests per week just very recently during the peak of the second wave (see Fig. 1). POC-based rapid testing can help to accelerate result output and reduce the burden on central laboratories. Dr. Rossier pointed out that POC testing can also help prevent lab personnel and instruments from being contaminated with contagious material. He concluded that in case of frequent monitoring, home testing, sample instability or in emergency situations, use of POC devices make sense, but each use case needs to be carefully evaluated and validated.

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2. Comparative Analysis of Automated Cell Counts in Oncological Patients: Reliable Results of Point of Care Blood Impedance Measurements and Pitfalls in MDS/AML

“Reducing turn-around time (TAT) with a POC device can also be important in a University Hospital situation” explained **Dr. Sabine Blum** from the Centre hospitalier universitaire Vaudois (CHUV) in Lausanne. For instance, blood cell counts for patients coming in for therapy can be rapidly performed in a POC manner, which accelerates the decision-making process and thus reduces

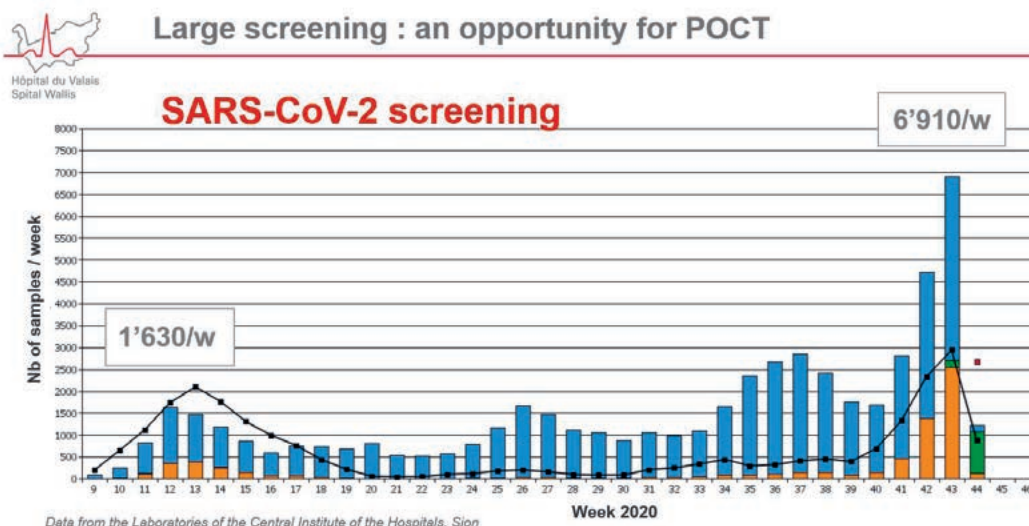


Fig. 1. Number of SARS-CoV-2 RT-PCR tests performed per week at the Institut Central des Hôpitaux (ICH) in the Valais during the year 2020. The blue bars indicate negative, orange positive and green pending results. A day prior the symposium event the Swiss Confederation approved the use of rapid immunological tests in Switzerland which should help address capacity challenges of the central laboratories. (Graphic by Dr. Alexis Dumoulin, Hôpital du Valais, Sion).

patient waiting times. She explained that for special settings such as in oncology, studies must show the suitability and robustness of the POC device. In the specific study she managed, all patients scheduled for chemotherapy and transfusion support over a period of 5 months were tested for haemoglobin, white and red blood cells and platelets with a direct current (DC) detection method. The haematology analyzer was linked to the central laboratory information system and gave a warning when values were out of range, *i.e.* required validation. These specimens then were also tested on a central laboratory instrument (in venous whole blood versus finger prick used with the POC device). Over 1500 samples were analyzed and no discrepancy with haemoglobin values were observed between the two systems used. However, with leucocyte and platelet measurements, there were instances of discrepant results, where the situation had to be clarified with microscopic analyses and central lab measurements were critically important for confirmation and correction. Dr. Blum concluded that POC testing devices are reliable and helpful in clinical care, but for special patient populations (such as haemato-oncological ones with low blood cell counts) reliable, highly precise performance is particularly important. She also highlighted, similarly to the ‘pre-analytical issue’ raised by Dr. Rossier, that physicians lacking training in laboratory medicine and relying only on the result print-out of the POC device, without consulting central lab results, may in some instances “post-analytically” draw wrong conclusions. This shows how important it is to embed POC testing in an overall workflow process.

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3. Improving Diagnostic for Infectious Diseases in Low- and Middle-income Countries: From R&D to Access via Validation

There are no borders for viruses such as SARS-CoV-2, which can critically affect also low- and middle-income countries (LMICs). It is estimated that 500 million tests will be needed over the next 12 months in LMICs. “Securing access to and deployment of affordable, quality point-of-care tests in these countries is one of the missions of the Geneva-based Foundation for Innovative New Diagnostics (FIND), especially within the context of the Access to COVID-19 Tools (ACT)-Accelerator partnership”, said **Dr. Kavi Ramjeet**, Technology Scouting Lead at FIND, in his introduction. He emphasized the importance of using antigen rapid diagnostic tests (RDTs) – especially the new generation of tests which show better performance – as a complement to current molecular tests. These RDTs can be made available at 5 USD or less. In early 2020, only a handful of antigen RDTs were launched or in development stage, but by the end of October 2020 more than 108 manufacturers of antigen RDTs (for visual read-out) had surfaced, 60 of whom had products in the validation and regulatory approval stage. While most of the tests so far use nasopharyngeal and oropharyngeal samples, newer ones are based on nasal and saliva sampling. Dr. Ramjeet also provided data on products that have shown sensitivities well above the WHO target product profile (TPP) requirement of 80% sensitivity and 95% specificity. With regards to molecular diagnostic tests, most products on the market are not instrument-free and are too costly for LMIC markets. In summary, the diagnostics arm of ACT-Accelerator provides all the important elements – guidance on the use, accelerated R&D, initial supply of rapid tests, funding – to support the launch, country uptake and scale-up of rapid tests for COVID-19.

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4. Point of Care Tests for Preeclampsia

“Preeclampsia (PE) is a dangerous condition and a leading cause of death in pregnancy throughout the world”, **Dr. Mathias**

Wipf, CEO of MOMM Diagnostics explained, “with 2–8% of all pregnancies affected, leading to 500’000 infant and 75’000 maternal deaths every year”. The condition is primarily defined by its symptoms, which are elevated blood pressure and proteinuria as well as many other non-specific symptoms. The origin is thought to be placental dysfunction. There are not many measures that can be taken: Aspirin medication to reduce the onset of PE and arranging the delivery. Dr. Wipf underlined that diagnosis is important before the disorder develops and two biomarkers – placental growth factor (PIGF) and the soluble fms-like tyrosine kinase-1 (soluble part of the receptor, sFlt-1) – are becoming increasingly important in this context. Essentially, in PE the balance between these two biomarkers is out of range. The goal of MOMM Diagnostics is to develop a POC diagnostic test based on these biomarkers for use at the obstetrician office as routine check-up tool. The so-called eFlow technology combines a cartridge-based lateral flow assay (LFA) technology with an electrical sensor and a hand-held reader that allows quantification of these low abundant biomarkers in a single drop of blood. The electrical sensor that uses an enzyme-linked signal amplification, is crucial to support the improved analytical sensitivity (LOD), quantification accuracy and dynamic range relative to other read-out modalities. Dr. Wipf summed up by stating that MOMM Diagnostics is currently at a feasibility prototype stage planning for *in vitro* studies in 2021 and clinical validation by Q4 2022.

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5. Innovative Diagnostics: Sensor Solutions for Resource-limited Settings

“POC Diagnostics can help address multiple aspects such as costs, staff capacity, irregular supply, infrastructure access, patient empowerment and reactive versus preventive and predictive medicine” begun **Dr. Samantha Paoletti** from the CSEM. However, combining test accuracy with rapidity, portability and user friendliness is not trivial, but essential, should not only trained doctors, nurses, pharmacists and caregivers, but also patients themselves be taught to use these tools. Dr. Paoletti also stressed the importance of sample preparation and fabrication techniques, both being critical for performance and cost-effective manufacturing down the road. She then introduced a new project at CSEM on migrant health monitoring (in collaboration with the Swiss Tropical and Public Health Institute) where they employ printed electrochemical sensors for urine analysis. In a broader context this project called “Novel Integrated Interactive Platform for Diagnosis and Surveillance of Diseases among Migrants (NIIDS)” also includes a serodiagnostic protein array against 16 febrile illnesses, a new PCR platform and a structured questionnaire to complete the screening approach. The urine analysis cartridge developed by CSEM combines four sensors for ions, metabolites and small proteins, calibration buffers and a fluidic system. To conclude her presentation Dr. Paoletti also mentioned the new NTN Innovation Booster ‘Cell Insights for Life (CI4L)’ that is being prepared for submission to Innosuisse and aims at using microphysiological systems (MPS) to accelerate innovation in various sectors including diagnostics.

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6. A Unique Lateral-flow Approach to Detect SARS-CoV-2 Neutralizing Antibodies

During the first wave of the COVID-19 pandemic in spring 2020 it was estimated from epidemiological models that the true number of infections were 2- to 10-fold higher than reported. The percentage of positive PCR tests allows a certain estimation; however, reliable antibody tests can help determine the true numbers. While not reliable during the early acute infectious

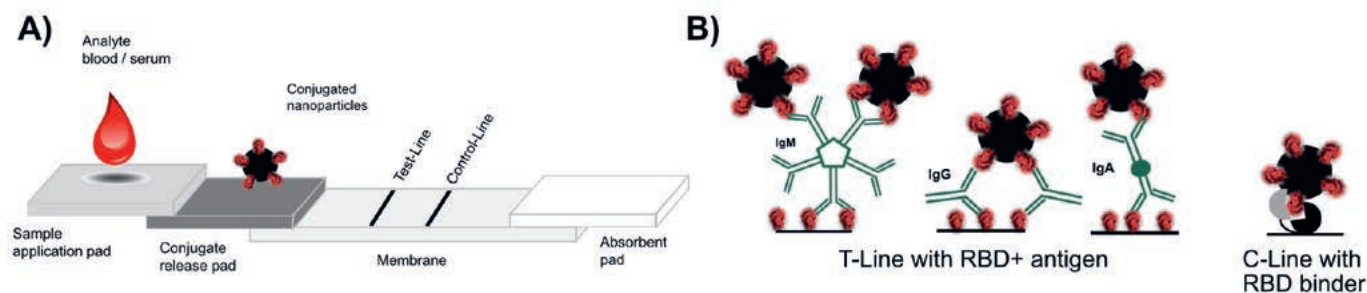


Fig. 2. A) General set-up of the Quantum Blue® SARS-CoV-2 RBD+ lateral flow test. RBD+ conjugated nanoparticles reside on the conjugate release pad. B) RBD specific antibodies of various isotypes cross-link RBD antigen on the test line with nanoparticles, while a synthetic binder against two RBD epitopes captures remaining RBD conjugated nanoparticles on the C-line. (Graphic by Christian-Benedikt Gerhold, BÜHLMANN Laboratories, Schönenbuch).

phase – where RT-PCR and antigen tests are applicable – antibody tests are useful approximately 10–13 days after symptom onset and beyond. In his presentation **Dr. Christian-Benedikt Gerhold** from BÜHLMANN Laboratories however showed data from FIND, where the majority of LFA-based rapid tests, both antibody and antigen, demonstrated insufficient sensitivity, *i.e.* less (and some considerably less) than 90%. “Antibodies targeting the spike protein – specifically the receptor binding domain (RBD) – of SARS-CoV-2 are thought to be neutralizing antibodies, preventing entry of the virus into the cell *via* the ACE2-receptor”, Dr. Gerhold explained. In their LFA, recombinant RBD as viral antigen is immobilized on the test line of the assay as well as conjugated to the nanoparticles. RBD-recognizing antibodies bind to both T-line and nanoparticles and, hence, become visible in this test set-up (see Fig. 2). On the control line, synthetic nanobodies (‘sybodies’) that recognize RBD are blotted, which eliminates the need for helper nanoparticles typically used with LFA. During a benchmark evaluation, BÜHLMANN’s Quantum Blue® SARS-CoV-2 RBD+ product showed a specificity of 99% and sensitivity of slightly less than 90%. A closer look at the false negatives with commercial ELISA revealed low antibody titers or presence of nucleocapsid (*i.e.* non-neutralizing) antibodies. Dr. Gerhold summarized that the validation of Quantum Blue® SARS-CoV-2 RBD+ product is almost complete and that a correlation study with neutralizing antibody titers from 200 RT-PCR positive serum samples is planned. He also highlighted that this new rapid test could be useful to monitor successful (prolonged) immune response – impairing a secondary infection – after RBD-based vaccination.

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7. The Future of Diagnostics in the Hand of Patients?



Keynote speaker
Dr. Markus Essenpreis
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“I am really passionate about this topic of the patient being in the center of the care process”, begun **Dr. Matthias Essenpreis** from Roche Diagnostics, his symposium keynote speech. “and I feel we are at a very special moment in time where there is a big opportunity to bring care into the hands of patients and redefine diagnostics in the hands of patients.” Referring with a smile to the archetypical and futuristic POC device – the tricorder used by Dr. McCoy on Star Trek expeditions that provides all and every information needed for medical decision making – he expressed his doubt that non-invasive approaches will answer all of today’s and tomorrow’s diagnostic needs.

Blood contains so much information, thus will keep on being an important basis for medical decision making, and with refer-

ence to COVID-19 and associated diagnostic tests, puts us back into today’s reality. Dr. Essenpreis also reminded us of the numerous, factory-like infrastructures – high-throughput systems in clinical laboratories – that allow deployment, for instance, of SARS-CoV-2 tests at scale and thus represents the backbone for diagnostic needs during a pandemic. This is certainly not POC. But blood glucose monitoring for the management of diabetes and coagulation testing to dose anti-coagulants certainly are value-proven POC diagnostic solutions. Fit for purpose! However, data aggregation over time and smart analytics are architecturally the 4th level (after the sensor, chemistry and communication technology) that really help understand the data. Continuous blood glucose monitoring with a sensor mounted on the body is an example where trending data is obtained for improved patient care. Parents, for instance, can see *via* their smartphone how their child’s measured values change. Dr. Essenpreis also mentioned Babyscripts™, an educational tool for pregnant women and new mothers, that allows an interaction with the platform and with physicians, generating useful data to support women with the right diagnostic information and care when they need it. Resuming the topic of COVID-19, Dr. Essenpreis asked, “Who of you would have thought a year ago that in Switzerland 2 million people would actually use an app on their smartphone to track who they were in contact with?” There is probably evidence eventually that this app saves lives and reduces infections. “Over the last nine months something else has been happening”, continued Dr. Essenpreis. Telehealth services have witnessed a surge during the pandemic. People could simply not go to see their doctor and telehealth was the only way doctors could continue providing their routine healthcare services especially during the lockdown period. There will be no way back, physicians have understood this to be convenient, safe and it works for the purpose with their patients who on their end also had positive experiences on telehealth platforms. Dr. Essenpreis concluded his inspiring keynote lecture and analysis with three hypotheses: 1) Sensors and wearables create valuable data streams for diagnosis and disease management, 2) emerging evidence for patient centric, digital solutions will change clinical practice, and 3) novel platform solutions will drive use cases with data driven approaches at scale.

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8. Using Blockchain Technology for Securing, Accessing and Verifying POC Data

Facilitating trust in the diagnostic process and patient data, *e.g.* by preventing tampering of data is very important. The COVID-19 pandemic had a major impact on digital health. Blockchain is like a distributed system (neither centralized nor decentralized) with no governing body, no single point of failure and with an infrastructure running 24/7. It is immutable, *i.e.* you

cannot change a block that previously was placed as a block in the chain, and it is transparent. This all makes it resistant to fraud. “What goes into the block is the hash of the previous block”, explained **Dr. Eberhard Scheuer** from Centiva Health, “and if you were to change a single digit in the block the whole hash of the past would not be the same anymore.” The process is associated with a time delay due to the decision to accept the new block and the broadcasting of a network node to the others, so that a new block can be added to each node. The system maintains itself, so this can be beneficial in a POC diagnostic setting and is also globally accessible, whereby the patient can control access to their data in the decentralized network. Dr. Scheuer mentioned the example of granting people access to locations (e.g. buildings) based on health status (e.g. via PCR, antigen or antibody test results or vaccination status) to ensure everyone’s safety. The 2-component solution being tested in several European countries currently provides an ‘open health certificate registry’ (tamper-proof digital certificates of e.g. antibody tests, independent verification via block chain and integration into existing systems such as lab systems and apple wallet for display) and a ‘health pass’ that presents the registry information and verification of certificates as well as user-controlled data. Practically this means that 1) the laboratory or healthcare professional generates an attestation (e.g. QR code) of the POC test, 2) the person receiving it creates a certificate on the smartphone, 3) the proof-of-existence of the attestation is written on the blockchain, 4) the app displays the attestation on the phone, 5) for instance at the airport the attestation is verified via blockchain, and then 6) the person can be granted or denied access. Of course, there are many other use cases, concluded Dr. Scheuer, for instance to assure safety when accessing retirement homes, workplaces, hospitals and events.

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9. Putting COVID Testing into Context: Understanding User and Community Needs for Meaningful POCT during the Lockdown Relaxation Phase

Testing for COVID-19 can also be used as a tool to manage confinement measures. Especially rapid POC testing combined with tracing (via a mobile app) and mandating of isolation can help to reduce the reproduction number thus infection incidence. “But what exactly are the user and community needs for meaningful POC diagnostics tests?”, asked **Dr. Adriano Taddeo** from the Institute of Virology and Immunology (IVI). Can these tests be helpful in the lockdown relaxation phase? In a study run at the HES-SO Valais-Wallis, SARS-CoV-2 antibody tests were used to identify potentially immunized people and plan the return to work. The tests were performed by 2nd and 3rd year students of the School of Health Science after having been briefed and trained (on the principles of immunology and of the test, how to use it and how to interpret the results and on hygiene rules). 100 HES-SO Valais-Wallis employees volunteered for testing and finally 50 were selected based on known PCR test status or symptoms and a certain number that had not been tested. The evaluation included usability aspects (execution efficiency, observed errors, system usability score/SUS) and a comparison to three commercial immunoassays performed at the central laboratory of the hospital in Sion. In summary there was not a big difference in the assay performance between the four tests, and the rapid test evaluated showed a specificity of 100% and a sensitivity of 67%. The latter somewhat poor result was mainly due to pre-analytical handling errors, although the users considered the test to be easy to use with a turnaround time of less than 4 minutes. Sampling (i.e. collection of enough blood) actually was the primary problem observed with all users, and result interpretation also needed clarification by experts. In conclusion, Dr. Taddeo confirmed

what Dr. Rossier in his opening lecture stated: “A POC diagnostic test should always be secondary to the clinical evaluation by a physician and, not necessarily the test itself, but the usability issues can be a significant source of errors!”

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10. Exhalomics & Laser Spectroscopy

Breath analysis and odour have a long medical history. Feeling “obliged” to refer to COVID-19 pandemic too at this symposium, **Dr. Lukas Emmenegger** from EMPA showed the example of trained dogs at the Helsinki airport sniffing coronaviruses from arriving passengers – so to say at POC. Indeed, small molecules such as nitric oxide, acetone, hydrogen and H₂O₂ in exhaled breath are examples of biomarkers for respiratory (asthma), metabolic (diabetes), gastroenteric and oxidative (cystic fibrosis) disorders, respectively. Now, exhaled breath is a challenging sample with volatile compounds being present only at ppq to ppm concentrations compared to nitrogen, oxygen, water vapor and CO₂ making up for almost 100% of the background signal. “What we want is to look at the systemic molecules coming from the organism, i.e. that have passed the blood-air barrier (alveoli), and that are a signature of a disease or a marker for a metabolic state” said Dr. Emmenegger. Mid-IR Laser spectroscopy has many attributes important to (POC) diagnostics: It is sensitive, selective, fast, quantitative, “calibration free”, compact and cost efficient. One of the most frequently used applications in the medical field is the detection of *Helicobacter pylori* that is linked to over 80% of gastric ulcers and that shows an infection rate of 25% in Western Europe. Urea labelled with ¹³C is metabolized by urease of *H. pylori* in the stomach to CO₂, absorbed into the blood and exhaled as ¹³CO₂. And as presented by Dr. Emmenegger, there are quite a number of commercial POC devices available on the market for this type of analysis mainly making sales – as typical for POC diagnostics – with consumables and test kits. Laser spectroscopy indeed is a promising diagnostic tool for applications in respiratory medicine, microbiology, clinical chemistry and pharmacology. Non-invasiveness and the lack of need for sample preparation makes it very attractive for POC diagnostics and positions it well between mass spectrometry (MS) and simpler sensors in terms of analytical performance and complexity. “Further exploration with regards to standardization and clinical validation, however, are still needed to tap the full potential of this technology”, concluded Dr. Emmenegger his very interesting talk.

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11. Harnessing Novel CRISPR Systems for Genome Engineering, Diagnostics, and Human Health

“Having all this genome sequence information available demands the capacity to actually manipulate it”, begins **Dr. Jonathan Gootenberg**, from the Massachusetts Institute of Technology (MIT), referring to harmful (e.g. single letter) mutations that afflict people like sickle cell disease, cystic fibrosis and eye degeneration. He points out that there are also mutations that protect humans such as the CCR5 mutation in the context of HIV. But also beyond healthcare, certain genetic traits can improve agriculture, e.g. against drought and insects, or by improving the yield. Nature’s diversity allows to use and further develop biochemical and molecular biological tools such as restriction enzymes, polymerases (PCR), viral vectors, fluorescent proteins, optogenetics, antibodies and of course gene editing tools such as CRISPR-Cas, which is a marvellous bacterial adaptive immune system. And Cas9 – the biochemical characterization that was awarded the 2020 Nobel Prize in Chemistry – is only a small slice of the CRISPR diversity, Dr. Gootenberg said. There are essentially two classes and six types of systems, with an important difference between the two classes: Class 1 uses multiple proteins

and Class 2 only single proteins like Cas9. So, the question is, how do we find more of these Class 2 proteins? “By computationally mining genomes for new systems based on Cas1”, he explained, this actually led to the discovery of a couple of new type V proteins today known as Cas12 (Cas12a, Cas12b, ...) and type VI, now known as Cas13, the latter being very interesting because it was targeting RNA. “We noticed that it cut the RNA not in a single place but in multiple”, Dr. Gootenberg highlighted. “In an interesting experiment back in 2016 we noticed that non-targeted (collateral) RNA – when added to the mixture of target ssRNA, crRNA and Cas13a – was cleaved also. This can be biophysically explained by the fact that the ‘molecular scissors’ are at the outside and when activated start to cut everything”. This was then turned into a detection system termed SHERLOCK (Specific High-Sensitivity Enzymatic Reporter Unlocking). Following an isothermal amplification step, *e.g.* recombinase polymerase amplification (RPA) for dsDNA or RT-RPA for RNA followed by an RNA transcription, the target is brought together with the Cas enzyme/crRNA/fluorescence molecule-tagged RNA probe which emits light upon collateral cleavage. SHERLOCK can be used for viral detection and strain discrimination, detection of bacterial antibiotic resistance genes, patient genotyping and detection of cancer-related mutations in cell-free DNA. By combing different Cas enzymes (*e.g.* Cas13 and Cas12a) and taking advantage of the substrate cleavage, *i.e.* ortholog base motif, preferences, multiplexing within the same solution becomes possible (see Fig. 3). For instance, a 4-plex assay combined 4 different enzymes with 4 different probes (each fluorophore emitting at a different wavelength) and 4 different RNA/DNA targets. Using a biotinylated probe also allows visual read-out when taking a LFA with a streptavidin line and anti-FAM (fluorophore) antibody conjugated with gold nanoparticles (AuNP). This way 10 copies of a Zika virus RNA were detectable with the naked eye. The FDA EUA approval for a COVID-19 rapid test that uses for the first time the CRISPR approach in May 2020 was a landmark. The test was further developed to become STOPCovid that includes a rapid sample extraction step and a single incubation step before read-out on an LFA. STOPCovid can be run on any setting by non-skilled person in less than 30 minutes.

In the second part of the keynote lecture, colleague **Dr. Omar Abudayyeh** from the McGovern Institute of MIT, turned our attention of CRISPR-Cas RNA-targeting tools to applications in the cell. RNA therapeutics can be based on RNA knockdown or base editing to correct mutations. “RNA editing allows temporal



Keynote speakers Dr. Jonathan Gootenberg and Dr. Omar Abudayyeh (McGovern Fellows at the Massachusetts Institute of Technology, Cambridge, USA).

modulation of protein activity”, explained Dr. Abudayyeh, “the effect can be reversed – by simply withdrawing medication – as compared to DNA-based editing that can have downsides you are not aware of.” In order to do the base editing with Cas13, one can use enzymes that normally deaminate adenosine to inosine such as adenosine deaminases acting on RNA (ADAR) enzymes. An ADAR recruited by a catalytically deactivated Cas13 (dCas13b) will recognize a dsRNA formed with the gRNA with single-base mismatch and then replace the base, *i.e.* convert A to I (REPAIR = RNA Editing for Programmable A to I Replacement). “But there is also a lot of editing off-target. That’s why we did a transcriptome-wide specificity study”, explained Dr. Abudayyeh. “We then did a rational mutagenesis based on structural information to tune the catalytic activity of the ADAR, *i.e.* to make it more specific to the mismatch bubble.” With the best mutant (REPAIRv2), one can go from 18’000 to 20 off-targets. “We also expanded the targeting range of RNA editing *via* directed evolution of ADARs to make dsRNA cytosine deaminases acting on RNA (CDAR) and eventually came up with RESCUE (RNA Editing for Specific C to U Exchange).” To conclude, RNA binding proteins have a wide range of applications, *e.g.* enhance or repress translation, skip or include exons, alter localization and epitranscriptomic modifications. “So, we really look forward to the RNA toolbox to continuously to be filled in, for therapeutic or diagnostic applications!”

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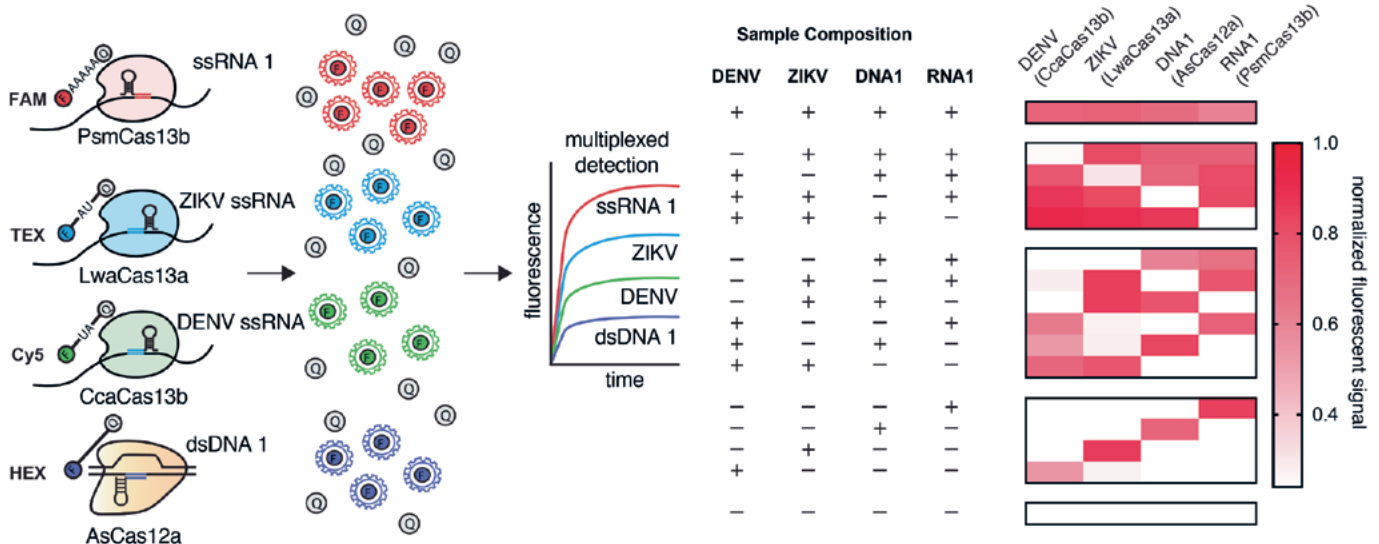


Fig. 3. Schematic of the SHERLOCK platform for in-sample 4-channel multiplexed nucleic acid detection with orthogonal CRISPR enzymes. (Graphic from keynote presentation by J. Gootenberg and O. Abudayyeh; [1]).

Satellite Event: Regulatory Challenges

The new *In Vitro* Diagnostic Regulation (2017/746 EU) represents a major challenge for start-ups as well as established companies. Thus, a satellite event to the symposium on regulatory challenges organized by **Prof. Didier Maillefer** from the HEIG-VD in Yverdon-les-Bains, was a useful complement to the main program. **Dr. Silvia Anghel** from Medidee in Lausanne gave an excellent overview of the regulatory requirements related to the *In Vitro* Diagnostic Regulatory transition. **Dr. Heike Möhlig-Zuttermeister** from the Notified Body BSI in Frankfurt, Germany, highlighted key aspects to consider on Clinical Evidence. Medidee's **Dr. Elena Lucano** further elaborated the expanding field of standalone software and smartphone apps used for diagnostic purposes. Before concluding the roundtable discussion moderated by Prof. Maillefer, **Dr. Claudia Solimeo Meneghisse** from Tecan in Männedorf presented an industry point of view on the challenges of the IVDR transition.

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[1] J. S. Gootenberg, O. O. Abudayyeh, M. J. Kellner, J. Joung, J. J. Collins, F. Zhang, *Science* **2018**, 360, 439.

The 4th edition of the Swiss Symposium in Point-of-Care Diagnostics will take place on 21st of October 2021 at the Davos Conference Center.

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Fig. 4. Collage with symposium speakers, young scientists shortlisted for a poster elevator pitch, session chairs and organizing committee members during the live *online* symposium event. (Photo by HES-SO Valais-Wallis).