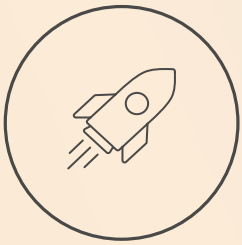
BRC CH Botnar Research Centre for Child Health

Annual Report 2020
Botnar Research Centre for Child Health

University of Basel ETH zürich

Supported by Fondation Botnar

Facts and Numbers



Jan 1, 2019
Start of Operations

4
Partner Institutions

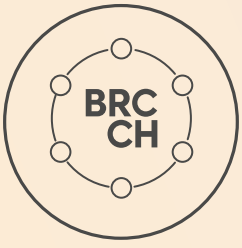
8
International Research Collaborations

42
Project Investigators

30.2
Mio CHF in Research Project Support

15
Research Consortia

19
Scientific Outputs



3
Research Programmes Launched

More than five million children under the age of five die every year, according to the World Health Organization.

Low- and middle-income countries carry a disproportionate burden of childhood disease and mortality.[1] Much of this burden could be alleviated with appropriate preventive measures and adequate therapies. Compounding this situation, emerging global health crises stress existing healthcare systems and highlight unprecedented public health challenges.

There is a critical need to develop and implement new, cost-effective and robust healthcare solutions and interventions for young people and those most in need. Innovative biomedical research and digital health technologies have the potential to address unmet medical needs around the world. However, to be impactful, solutions and interventions have to be context-specific and translatable.

In order to develop innovative, efficient and effective healthcare interventions and treatments for the most vulnerable worldwide, the University of Basel and ETH Zurich jointly founded the Botnar Research Centre for Child Health (BRCCH). This independent research centre is generously supported by the Basel-based Fondation Botnar.

Annual Report 2020
Botnar Research Centre for Child Health

A researcher examines a flow cell holding micro-amounts of samples, which is used in next generation sequencing techniques.

Dear colleagues and friends of the BRCCH,

Prof Georg Holländer
Director

Prof Sai Reddy
Vice Director

The BRCCH opened its doors two years ago at the start of 2019. In its first year, the Centre transitioned from concept to reality. This past year, the Centre started its ambitious research activities in partnership with the University of Basel, ETH Zurich, University Children's Hospital Basel (UKBB) and the Swiss Tropical and Public Health Institute (Swiss TPH).

The COVID-19 pandemic has recently occupied most of the world's attention, demanding resilience, patience, strength of purpose and optimism in these unprecedented times. The BRCCH was not exempt from this challenge. In further partnership with Fondation Botnar, the Centre spearheaded a rapid research programme in response to the pandemic. Our Fast Track Call (FTC) for Acute Global Health Challenges related to COVID-19 focused on Diagnostics, Immunology and Interventions. This effort helped us not only to advance our detection and understanding of the disease's pathogenicity, but also shaped designs for mitigating its devastating effects on livelihoods worldwide. In the autumn, the BRCCH hosted a webinar series to showcase the FTC programme and to present first results and progress of the research supported.

The BRCCH also joined efforts to create solutions to the pressing challenges of COVID-19 by participating in the VersusVirus Hackathon, a Swiss-wide effort to connect like-minded people and organizations to develop, scale and apply solutions in response to this pandemic. At the end of this exceptional year, we also initiated a collaboration with the European & Developing Countries Clinical Trials Partnership (EDCTP) to support COVID-19-related research activities across sub-Saharan Africa.

Additionally, the BRCCH directed its 2020 activities towards further defining its research strategy and created a fellowship programme for early career researchers. We prepared a launch for additional multi-year research programmes across the Centre's research remit. Moreover, we hosted our first public event, the BRCCH Spotlight Day.

This Annual Report provides you with a summary of the research expertly realised by our partners and funded by the BRCCH. This work ranges from early discovery research in the domain of basic biomedical sciences to work that translates therapies and novel forms of digital health support for the benefit of communities, especially those in low- and middle-income countries.

None of the past year's activities and milestones could have been achieved without the many discussions we have had with stakeholders, researchers and clinicians in the BRCCH research community. We sincerely thank our partner institutions for their continued commitment to and engagement in the health and well-being of young people. We also extend our gratitude to Fondation Botnar for their significant support and continued trust in the BRCCH to enable the best research for those most in need.

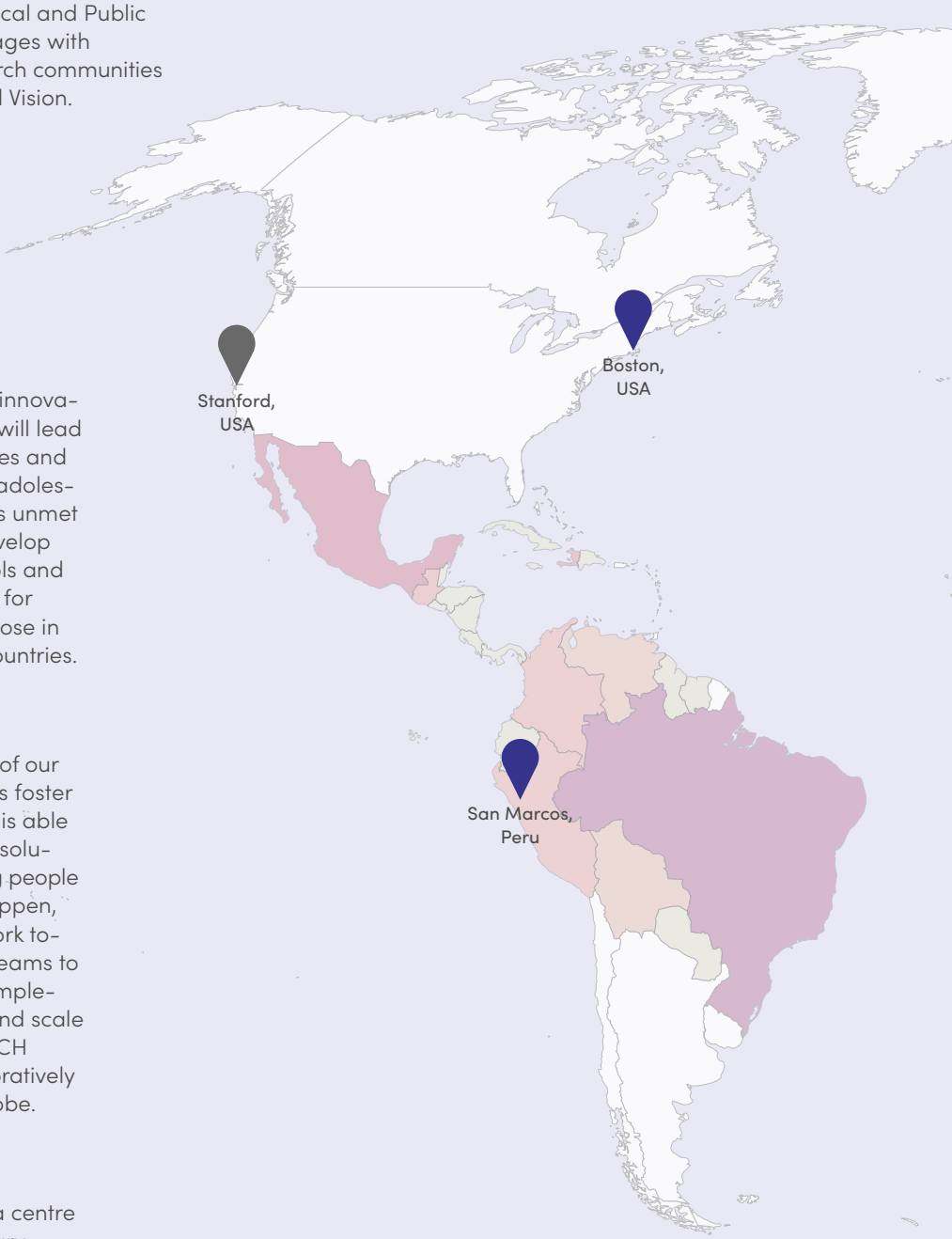
Therefore, it is with great pleasure that we present the BRCCH's 2020 Annual Report.

With our sincere regards,

Georg Holländer Sai Reddy

A Hub for Paediatric Research

The BRCCH is physically located in Basel, Switzerland. We maintain close ties with researchers at our four partner institutions: the University of Basel, ETH Zurich, University Children's Hospital Basel and the Swiss Tropical and Public Health Institute. In addition, the Centre engages with national and international networks of research communities in order to realize our Mandate, Mission and Vision.

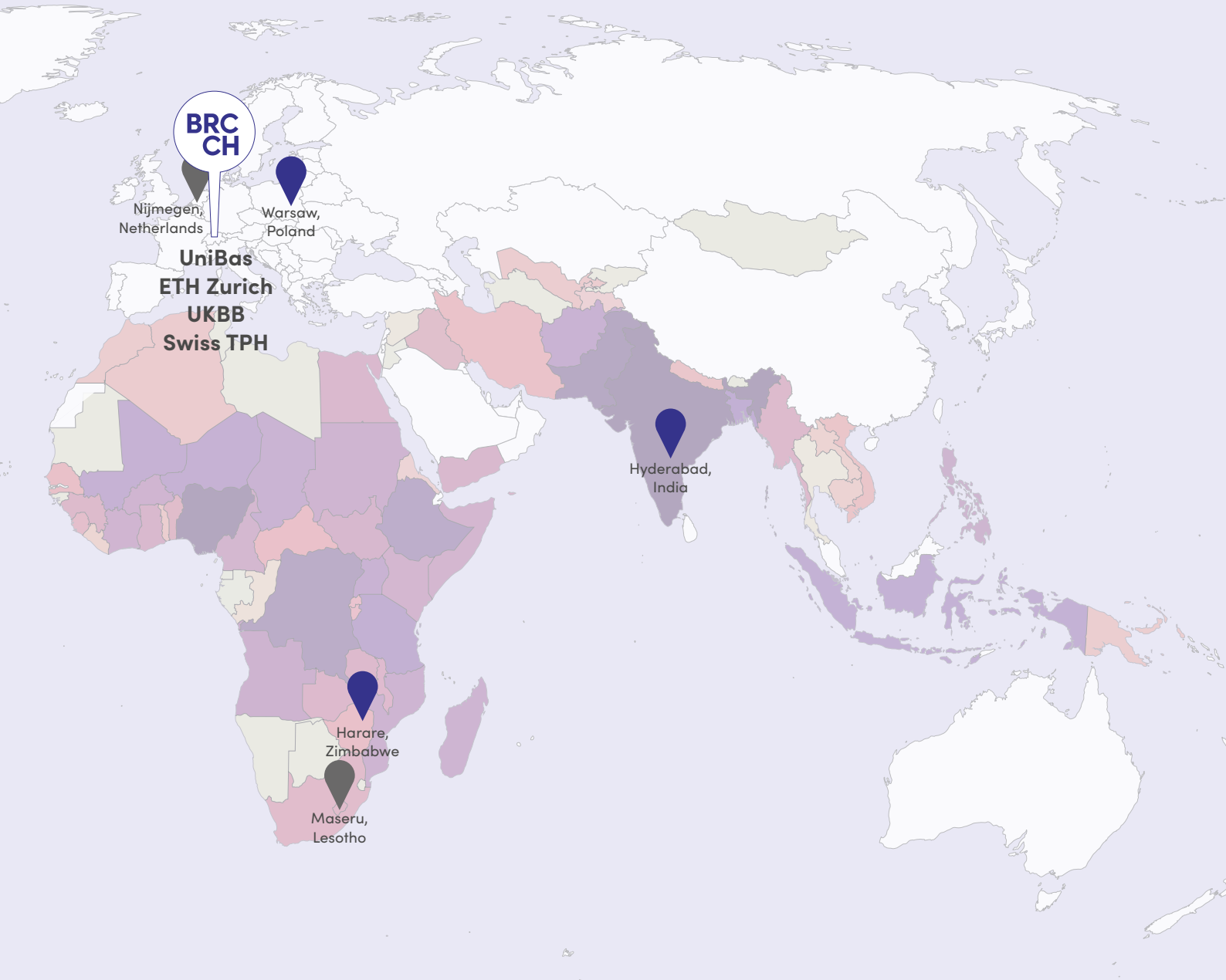


BRCCH collaborators and partners involved in:
Multi-Investigator Programme
Fast Track Call
(as of December 2020)

Our Mandate
is to drive outstanding and innovative scientific research that will lead to improved health outcomes and well-being in children and adolescents. The Centre addresses unmet medical needs, seeks to develop and improve diagnostic tools and designs novel interventions for young people, especially those in low- and middle-income countries.

Our Mission
is to embrace the expertise of our partner institutions and thus foster a research community that is able to develop new healthcare solutions for the benefit of young people worldwide. To make this happen, physicians and scientists work together in multidisciplinary teams to recognize medical needs, implement innovative research and scale feasible solutions. The BRCCH pursues these goals collaboratively with partners across the globe.

Our Vision
for the BRCCH is to create a centre which fosters multidisciplinary and translational research in order to address unmet medical needs in paediatric health. The objectives are to create novel solutions for the prevention, diagnosis and treatment of disease and to develop tools that can accurately predict their course. The BRCCH aims to become a crystallization point for national and international expertise in child health.

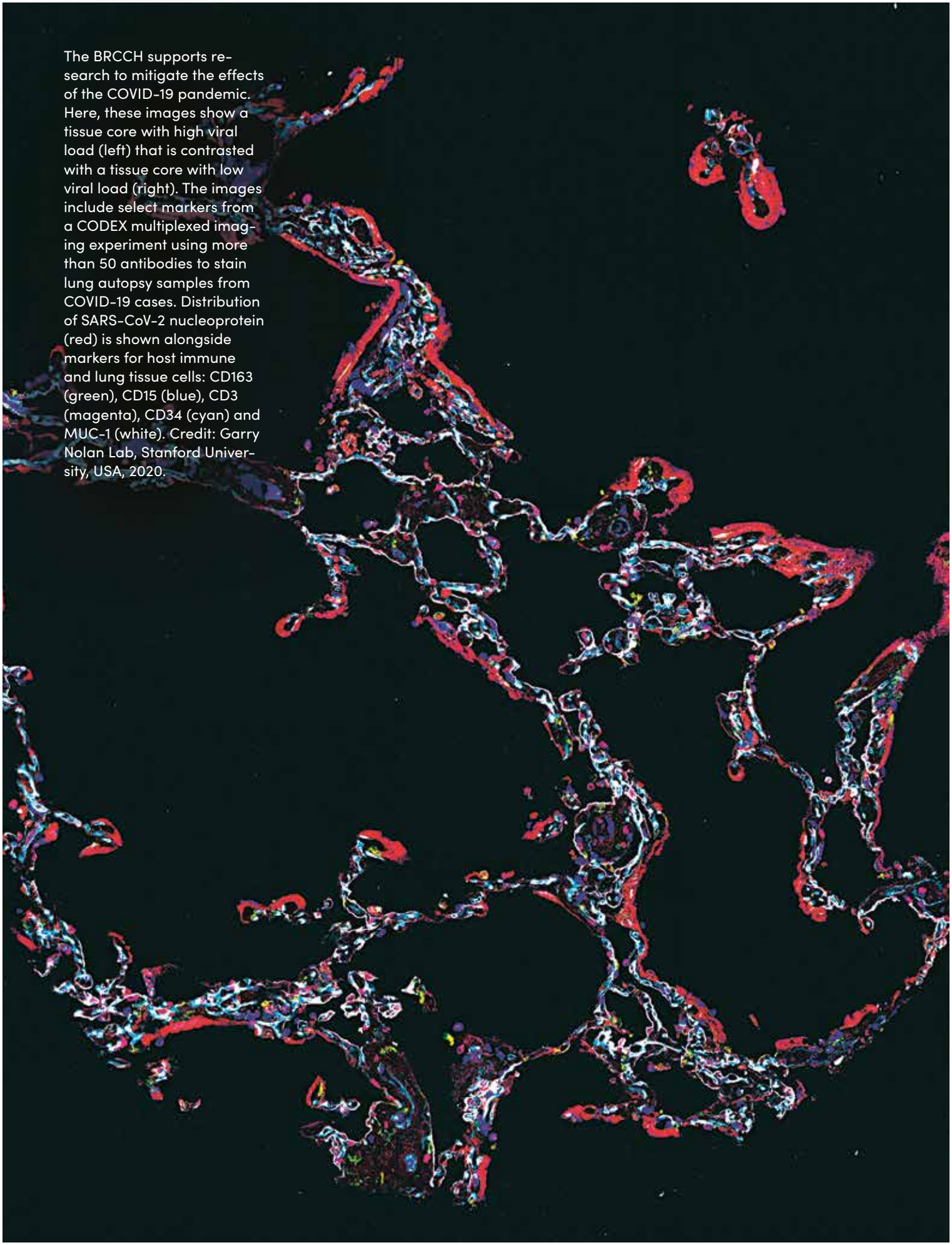


Estimated mortality of children under 5 years of age in 2017 across 99 low- and middle-income countries[2]

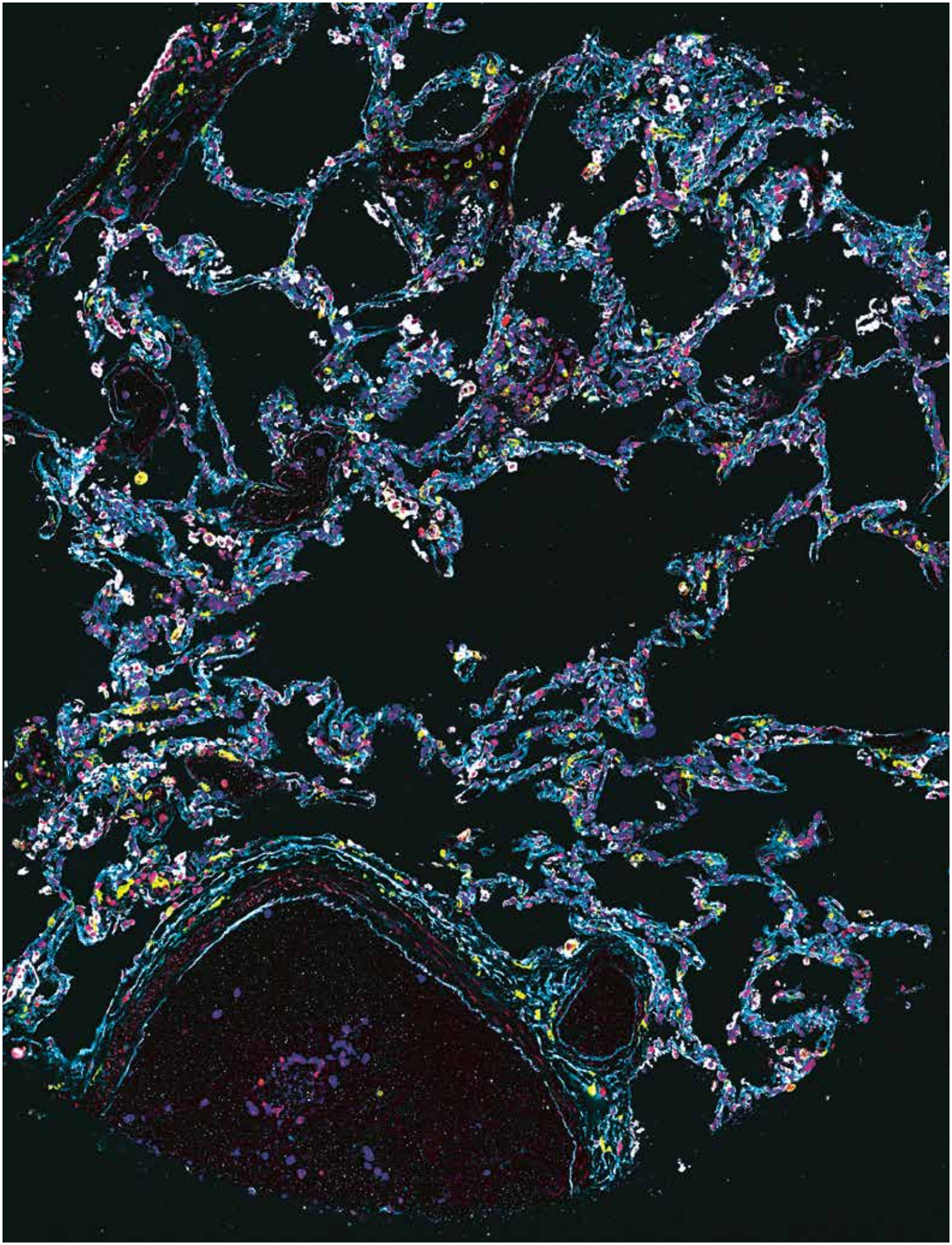
Number of deaths ($\times 10^3$)

> 500
200
50
5

Countries pictured in white were excluded from study



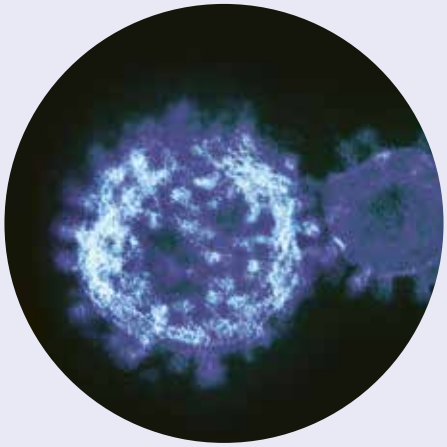
The BRCCH supports research to mitigate the effects of the COVID-19 pandemic. Here, these images show a tissue core with high viral load (left) that is contrasted with a tissue core with low viral load (right). The images include select markers from a CODEX multiplexed imaging experiment using more than 50 antibodies to stain lung autopsy samples from COVID-19 cases. Distribution of SARS-CoV-2 nucleoprotein (red) is shown alongside markers for host immune and lung tissue cells: CD163 (green), CD15 (blue), CD3 (magenta), CD34 (cyan) and MUC-1 (white). Credit: Garry Nolan Lab, Stanford University, USA, 2020.



2020 in Review

January
Spotlight Day

The inaugural BRCCH Spotlight Day marked the start of bringing the community together, both locally and globally, around the central mission of improving the health and well-being of children and adolescents worldwide. More than 200 visitors joined the BRCCH in Basel. Four BRCCH Multi-Investigator Programme projects (MIPs) showcased their research visions for the next five years. The event also featured three international keynote speakers: Prof Samuel Sia (Columbia University, USA), Prof Faith Osier (KEMRI-Wellcome Trust, Kenya and Heidelberg University Hospital, Germany) and Dr Alexander Finlayson (Nye Health and University of Oxford, UK).



March
COVID-19 Fast Track Call

In response to the emergence of COVID-19, the BRCCH, with additional financial support from Fondation Botnar, quickly launched a new research initiative to address several critical areas related to the pandemic. The Fast Track Call (FTC) initiative was designed to enable research that will help to mitigate medical and public health challenges in the short term and also contribute solutions that will lead to better preparedness and reduced global disease burden in the long term. The call for applications to the FTC circulated in March. Of the 73 research consortia that submitted project proposals in April, the international review panel recommended 11 projects. These projects were subsequently approved by the BRCCH Board and were able to begin their research activities in May. See page 22 for project descriptions and consortia details.
Credit: National Institute of Allergy and Infectious Diseases (NIAID).

April
Online Hackathon VersusVirus

The BRCCH contributed to the two-day online VersusVirus hackathon, where the goal was to develop digital or analogue prototypes to offer tangible solutions to counter the pandemic. The BRCCH helped with organizing the event along with 60+ teammates across Switzerland. More than 5000 people participated in 600+ teams to solve 200 challenges. The VersusVirus hackathon, under the patronage of the Swiss Federal Department of Home Affairs, was the largest hackathon and one of the largest collaborative online experiences in Swiss history.
Credit: #VersusVirus

June
International Webinar OneCleftSurgery

Dr Andreas Mueller and members of his MIP consortium contributed to global capacity building by co-leading a two-day training webinar related to the one-step cleft lip and palate surgery method. The international speakers and co-organizers included surgeons from Poland and Japan. The "1st International Webinar for One-Step Unilateral Cleft Lip and Palate Surgery Leading to Pure Primary Healing" was highly successful, with more than 1100 participants from 66 countries, and it was offered free of charge.

September
COVID-19 Research Webinar Series

The BRCCH organized and hosted an open access webinar series titled "Insights into COVID-19 Research" over three evenings in September. There was a great deal of public interest in this series, with more than 300 attendees from 46 nations across the world.

During the first two evenings, the webinar series provided an in-depth look at BRCCH research projects focusing on the diagnostics and immunology of COVID-19, as well as others focusing on novel medical interventions for the disease. Speakers included Prof Mirko Meboldt, Prof Andreas Moor, Prof Roland Regoes and Prof Janos Vörös (all from ETH Zurich), Dr Michael Osthoff (University Hospital Basel), Prof Melissa Penny (Swiss TPH) and Prof Thomas Erb (UKBB).

The third evening's webinar dipped into the global conversation about the challenges and latest developments in the race to respond to the pandemic, with a focus on low- and middle-income countries. Viewers heard first-hand from international experts about the current landscape of public health and how technology and partnerships spanning borders could meet current challenges in the pandemic. The panel included Prof Alain Labrique (Global mHealth Initiative, Johns Hopkins University), Dr Solomzi Makohliso (EssentialTech, EPFL), Prof Marcel Tanner (Swiss Academy of Sciences; Fondation Botnar) and Akhona Tshangela (Africa Centres for Disease Control and Prevention), and it was moderated by Dr Maxine Mackintosh (One HealthTech; Alan Turing Institute).

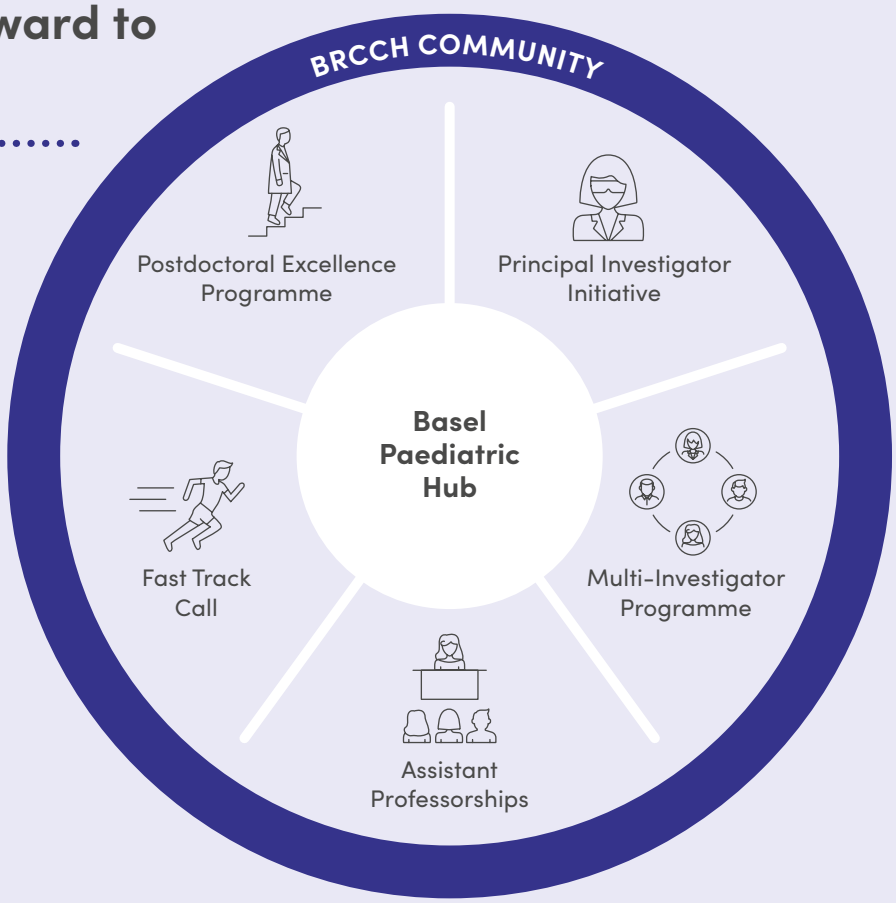
November
New Look for 2021 Office and Online

Many new things happened in the internal workings of the BRCCH. First, the BRCCH management team moved to a new office at Petersgraben 31, 4051 Basel, Switzerland, and it is looking forward to when it will be possible and safe to welcome guests and have in-person meetings once more. Second, the BRCCH launched its newly designed www.brc.ch website, with additional details about the Centre, the researchers involved and its latest activities. As part of the website, the BRCCH also introduced a new grants management portal: an online platform for the preparation, submission and review of applications and the subsequent management of awarded proposals.

October
Launch of Postdoctoral Excellence Programme

The BRCCH launched its third research initiative, the Postdoctoral Excellence Programme (PEP), in order to foster the next generation of scientific leaders who will conduct interdisciplinary and step-changing research to address critical unmet needs and challenges in global paediatric medicine and health. The call for applications was open to Host Principal Investigators from the BRCCH partner institutions with highly translational and ambitious proposals that they wished to bring to life together with talented and aspiring Postdoctoral Fellows. PEP applications were due in January 2021 and will undergo external evaluation by international experts. Credit: Joachim Pelikan, Swiss TPH

Here is what to look forward to in 2021



Research
The BRCCH eagerly awaits the onboarding of the first generation of successful postdocs in the Postdoctoral Excellence Programme. These fellows will be an important part of the BRCCH research community and together with students supported within other BRCCH programmes, they will represent the BRCCH's aim to support early career researchers. Additionally, the Centre will further expand and strengthen its research portfolio with the launch of the Principal Investigator Initiative. This programme will enable focused research projects that are aligned with the BRCCH Vision and led by one or multiple investigators from BRCCH partner institutions.

International Collaboration
At the close of 2020, the BRCCH successfully concluded discussion with the European & Developing Countries Clinical Trials Partnership (EDCTP) about opportunities for research collaborations between the respective COVID-19 research activities supported by each of the organizations. Parallel to the BRCCH FTC initiative, the EDCTP launched its own emergency mechanism to support research in sub-Saharan Africa to manage and/or prevent the spread of COVID-19. Both organizations aim to build shared international know-how in the pathogenesis, immunology and epidemiology of COVID-19, as well as to accelerate the development of new diagnostics and medical interventions for this disease, particularly in low-resource settings.

Community
The BRCCH will continue its efforts to form a research community. Building on the success of the Spotlight Day and its open access webinar series, the Centre is planning additional events in the second half of 2021, such as a follow-up on COVID-19 research efforts and offerings designed specifically for early career researchers.

Meet the Advisory Board

The BRCCH's activities benefit from the involvement of the members of the BRCCH Strategic Scientific Advisory Board (SSAB). The BRCCH is pleased to introduce the members here, some of whom have been advising the BRCCH since its operations began two years ago and some of whom joined the Centre this past year. Together, the members possess considerable complementary knowledge and know-how, and the BRCCH is grateful for their active engagement and expert advice.

Prof Marcel Tanner is president of the Swiss Academy of Arts and Sciences and a board member of Fondation Botnar. He is a director emeritus of the Swiss TPH and also a professor emeritus of epidemiology and medical parasitology at the University of Basel. His research interests include the fields of global health, epidemiology, health systems, infectious diseases and public health.

Elsbeth Müller is the former CEO of UNICEF (United Nations Children's Fund) Switzerland and currently serves as a board member of Fondation Botnar. During her tenure at UNICEF, she championed children's rights in Switzerland, oversaw the certification of many Swiss cities as "child-friendly communities" and was involved in international projects for the benefit of children's health and well-being.

Prof Christopher B Forrest is a professor of paediatrics at the Children's Hospital of Philadelphia (CHOP) and the University of Pennsylvania, USA. He is also the director of the Applied Clinical Research Center at CHOP. His research interests include global health, health information technology, comparative effectiveness research, delivery innovation and patient-centred medical homes.

Prof Edina Sinanovic is an associate professor and head of the Health Economics Division at the School of Public Health and Family Medicine at the University of Cape Town, South Africa. She has worked on the economic evaluation of healthcare interventions, economic considerations in vaccination and scaling up health interventions. Her current research focuses on evaluating the cost-effectiveness of alternative diagnostic and treatment interventions for TB, HIV and cancer.

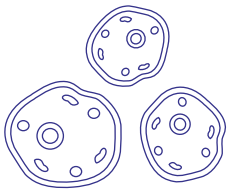
Prof Melody Swartz is the William B. Ogden Professor at the Pritzker School of Molecular Engineering at the University of Chicago, USA, where she holds a joint appointment in the Ben May Department for Cancer Research. She uses quantitative approaches in immunobiology and physiology in order to develop a deeper understanding of how the lymphatic system regulates immunity in homeostasis and disease, particularly in cancer and chronic inflammation.

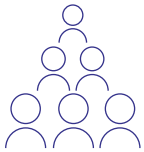
Prof Erwin Böttinger holds dual academic appointments as a professor of digital health and personalized medicine at the Hasso Plattner Institute and the University of Potsdam, Germany, and as a professor of medicine at the Icahn School of Medicine at Mount Sinai in New York City, USA. His interdisciplinary research in digital health and personalized medicine combines digital technologies with molecular and data sciences.

Credits: Elsbeth Müller: Fondation Botnar. Prof Melody Swartz: John D and Catherine T MacArthur Foundation.

Research Portfolio

In order to deliver on its ambitious goals, the BRCCH seeks to support a comprehensive research portfolio with projects that span from early-stage endeavours with significant innovative and translational potential to mature-stage projects focused on validation and implementation.

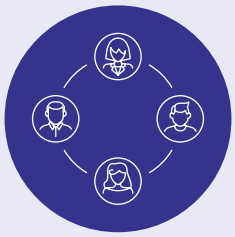




Early-Stage Research
The Centre's projects have significant innovative potential and in the long term, a high likelihood of translation and eventual implementation in low- and middle-income settings. These projects include endeavours that address relevant challenges associated with significant disease burden and/or societal implications in the Global South. The BRCCH therefore invests in scientifically outstanding early-stage projects that promise to deliver step-changing solutions.

Translational Research
These projects are positioned on the path to implementation at a stage where previously collected research findings can now be further validated at scale and translated into use-inspired solutions. Translational projects will advance early technology and engineering developments designed to improve diagnostics, disease monitoring or therapy. The realisation of these projects forms an essential element of the BRCCH's remit of implementing findings from basic science.

Mature-Stage Research
These projects test the feasibility, robustness and usefulness of methods and medical devices for the diagnosis, treatment, monitoring and predicted future course of diseases on a larger scale, in real-world settings and in consideration of specific contexts. BRCCH researchers work closely with international collaborators to test the effectiveness of methods and devices in their intended use and to investigate the feasibility of their uptake, especially under resource-constrained conditions.



Updates from the Multi-Investigator Programme

The Multi-Investigator Programme (MIP) projects are the first cornerstones in the BRCCH research portfolio. The programme forges multidisciplinary synergies between investigators from our four partner institutions and fosters international collaborations that will increase the likelihood of clinical translation and implementation worldwide.

Four projects are currently supported by the MIP initiative. They began their research activities in early 2020 and will run for five years. Each project has made significant progress towards its aims this past year, despite unanticipated delays and disruptions due to the COVID-19 pandemic.

Digital Support Systems to Improve Child Health and Development in Low-Income Settings

Overview. In many low- and middle-income countries, families living in remote areas often have insufficient access to healthcare and health-related services to adequately support their children's development in the first years of their lives. Digital tools, however, may help to fill this gap. This research will assess the efficacy and improve the performance of an interactive mobile phone-based application based on artificial intelligence. The aim is to further develop this digital tool to help parents best support their children's development in the first 100 days of life.

Update. During the past year, the project focused on further developing the digital platform to support early childhood development and began local testing at field sites in the San Marcos region of Peru. The team successfully completed a first review of all the platform's content and activities, developed new modules and began piloting the Afini-digital platform with local mothers. Ethical approval for the project's study protocol was obtained from the ethics boards in Peru and in Switzerland. Additionally, the team designed a theory of change for the project, identified the first set of key measures to be used in the study and is currently writing a review article on the use of digital early childhood interventions in low- and middle-income countries.

Collaborators: ETH Zurich: Ce Zhang. Cayetano Heredia University, Peru: Stella Hartinger Peña. Harvard, USA: Dana McCoy. Afinidata: Andreana Castellanos.

Image: A girl living in a mountainous region of Peru. Credit: Daniel Mäusezahl & Stella Hartinger Peña.

Investigators

Günther Fink
Swiss TPH

Daniel Mäusezahl
Swiss TPH

Burden-Reduced Cleft Lip and Palate Care and Healing

Overview. Orofacial clefts, or cleft lip and palate, are the most frequent craniofacial malformations in newborns, with no existing effective preventive measures. This project aims to develop a smartphone image-based method for computing a 3D shape image of the cleft. This enables three new treatment regimes: 1) a quantifiable correlation between the cleft shape, the optimal time point for surgery and its outcome; 2) a fully digital fabrication of individualized orthopaedic palatal plates that help to reduce the size of the cleft before surgery; 3) the closure of the malformation in a single surgical intervention instead of multiple interventions.

Update. The project has made progress by digitizing historical data on malformations by 3D scanning all of the available palatal plaster casts in Basel. Additionally, the team has also established a new, risk-free, faster and more accurate way of acquiring the 3D digital palatal data by using an intraoral scanner. So far, the malformations of more than 320 individuals have been digitized. Computational shape analysis of the increasing number of digitized malformations continues to improve the accuracy of the established 3D intraoral palatal model.

Collaborators: GSR Institute of Craniofacial Surgery, India: Srinivas Gosla Reddy. Institute of Mother and Child and Formmed Clinic, Poland: Andrzej Brudnicki. Disney Research Studios: Markus Gross.

Image: A plaster mould of a dental impression of a child's cleft palate sits in a machine which will 3D scan it and thus produce a digital copy. Researchers will use the digital data from this mould and others like it in machine learning algorithms for shape computation.

Investigators

Andreas Mueller
University Hospital Basel and University of Basel

Barbara Solenthaler
ETH Zurich

Living Microbial Diagnostics to Enable Individualized Child Health Interventions

Overview. Millions of children annually do not reach their developmental potential, which is predominantly due to infectious diseases as well as to malnutrition and related disorders. Microbiota in the gastrointestinal tract, or gut, often change in response to illness or disease in the body. Monitoring such changes could inform us about the current health status of the body. This research project aims to engineer bacteria to serve as a non-invasive living diagnostic to record these changes in the gut and thereby provide a basis for individualizing and improving health interventions for children and adolescents worldwide.

Update. This project builds upon recent methods developed by the Platt lab for engineering a bacterium using CRISPR-based technology. Progress has been made in understanding how the engineered bacteria can safely traverse animal gastrointestinal tracts while faithfully sensing and reporting on diverse and fluctuating intestinal environments. The project has also been collecting longitudinal samples from mothers and babies living in Zimbabwe, which the researchers will analyse in the future with the aim of gaining further insight into the impact of malnutrition and related disorders on gastrointestinal function in children.

Collaborators: University of Bern: Andrew Macpherson. University of Zimbabwe, Zimbabwe: Kerina Duri.

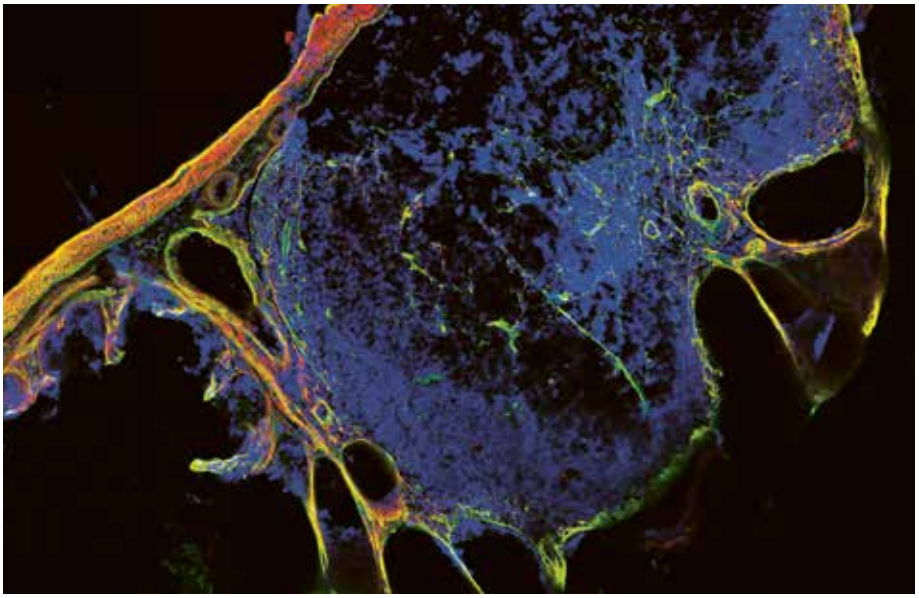
Image: A researcher in the Platt lab uses bacteria to engineer proteins with enhanced functionality. These methods are used to bioengineer bacteria to improve the efficiency of a novel technique called Record-seq.

Investigators

Randall Platt
ETH Zurich

Dirk Bumann
University of Basel

Uwe Sauer
ETH Zurich



Precision Microbiota Engineering for Child Health

Overview. Two very serious diseases of newborns – namely, inborn errors of metabolism and neonatal sepsis – currently have high mortality rates, long-term consequences for child development and limited treatment options. This consortium seeks to develop novel intervention strategies for these diseases using advancements in microbiota bioengineering. The project aims to alter the metabolism of the microbiota or to replace "bad" bacteria or functions in the gut microbiome with "desirable" ones. Overall, the research will generate fundamental insight into microbiota, as well as preclinical insight into therapy efficacy and safety.

Update. This project has made steady progress across multiple work packages. The team completed preparations for two clinical studies to begin in January 2021. The team continues to develop a microbiota-controlled mouse model for studying inborn metabolic disorders, as well as to expand its available microbiota-targeting vaccines and CRISPR-based *in situ* genetic engineering. Furthermore, the project has validated a range of techniques required for the analysis of the impact of microbiota engineering on disease severity (brain damage, metabolic organ damage, intestinal damage) and for microbiota analyses.

Collaborators: ETH Zurich: Christian Wolfrum. University Hospital Basel: Adrian Egli. University Children's Hospital Zürich: Matthias Baumgartner, Johannes Häberle, Sean Froese, Johannes Trück. University Hospital Zürich: Giancarlo Natalucci. Paul Scherrer Institute: Martin Behe.

Image: Microscopic view of a cross-section through a lymphoid structure in the mouse cecum, showing extracellular matrix in green and red and cellular nuclei in blue. Credit: Ronja Rappold.

Investigators

Emma Wetter Slack
ETH Zurich

Johannes Bohacek
ETH Zurich

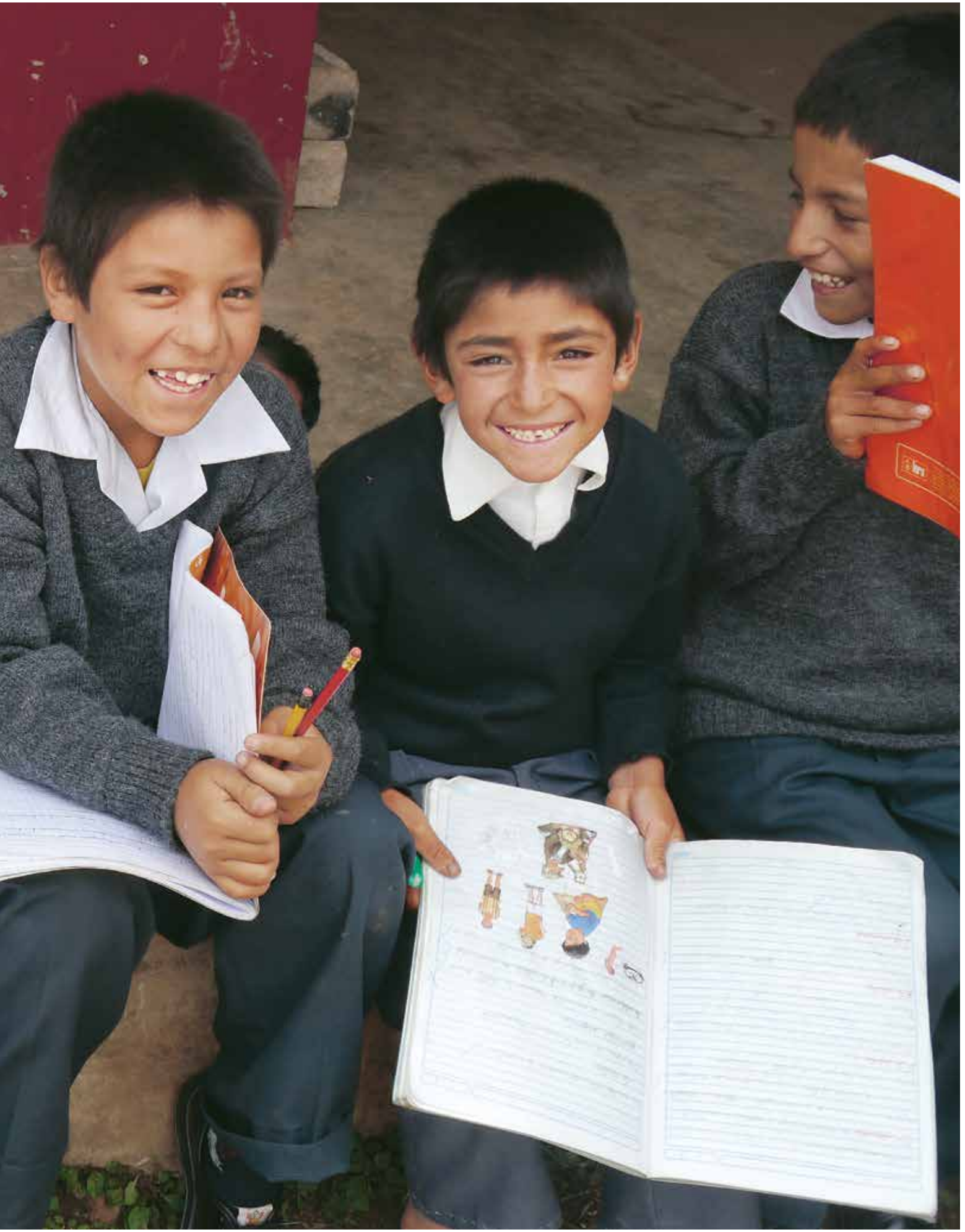
Médéric Diard
University of Basel

Shinichi Sunagawa
ETH Zurich

Viola Vogel
ETH Zurich

Ferdinand von Meyenn
ETH Zurich

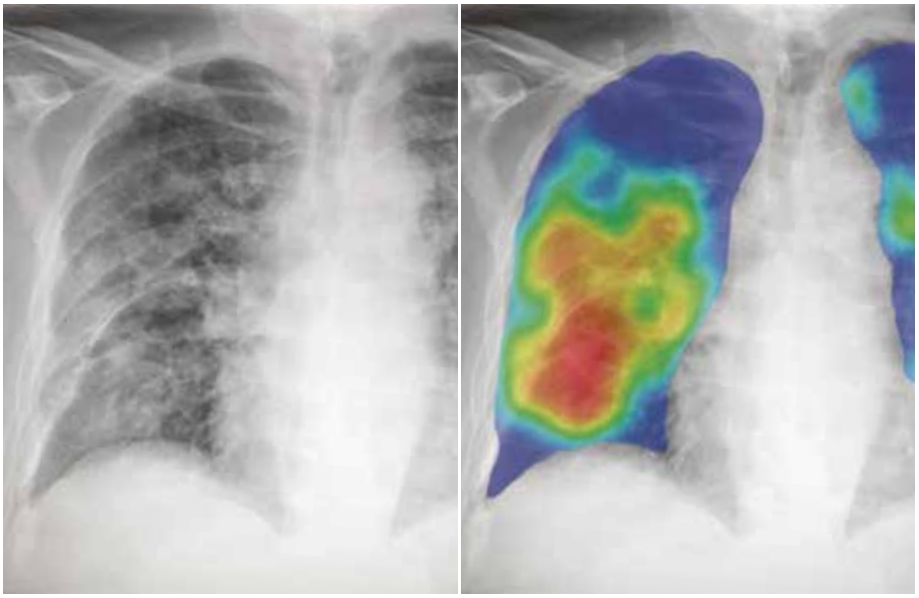
The BRCCH enables multi-disciplinary and multi-institutional research that aims to promote the health of young people worldwide, such as these students pictured here in San Marcos, Peru. BRCCH researchers are working together with international collaborators to enhance a mobile application for improving the well-being and life-course of children growing up in low-resource or remote settings where healthcare infrastructure may not be readily accessible. Credit: Daniel Mäusezahl & Stella Hartinger Peña.



Fast Track Call: COVID-19 Research

The BRCCH's mandate is to drive the development of innovative and step-changing healthcare solutions for those who are most in need. In response to the COVID-19 pandemic, the BRCCH, together with additional financial support from Fondation Botnar, created an FTC for Acute Global Health Challenges. The initiative served as a rapid emergency response to the unprecedented damage to the health and well-being of communities worldwide.

The overall objectives were both to quickly enable research that will help to mitigate medical and public health challenges in the short term and also to contribute tangible solutions that will lead to better preparedness and reduced global disease burden in the long term. Eleven research consortia were awarded grants to conduct projects of 2.5 years' duration, starting in May 2020. The projects cover research in the areas of Diagnostics for COVID-19 (five projects), Human Immune Response to COVID-19 (three projects) and Medical Interventions and Disease Management for COVID-19 (three projects).



MistraL: Mitigation Strategies for Communities with COVID-19 Transmission in Lesotho Using Artificial Intelligence on Chest X-Rays and Novel Rapid Diagnostic Tests

For mitigation strategies to be effective and efficient against COVID-19, they must be context-specific and take local conditions into account. In low- and lower-middle-income countries, limited resources and fragile healthcare systems often dictate what is feasible. In this project, researchers combine artificial intelligence, portable chest X-ray machines and antigen-based diagnostic tests to enable and improve diagnosis of COVID-19 patients in settings with limited resources.

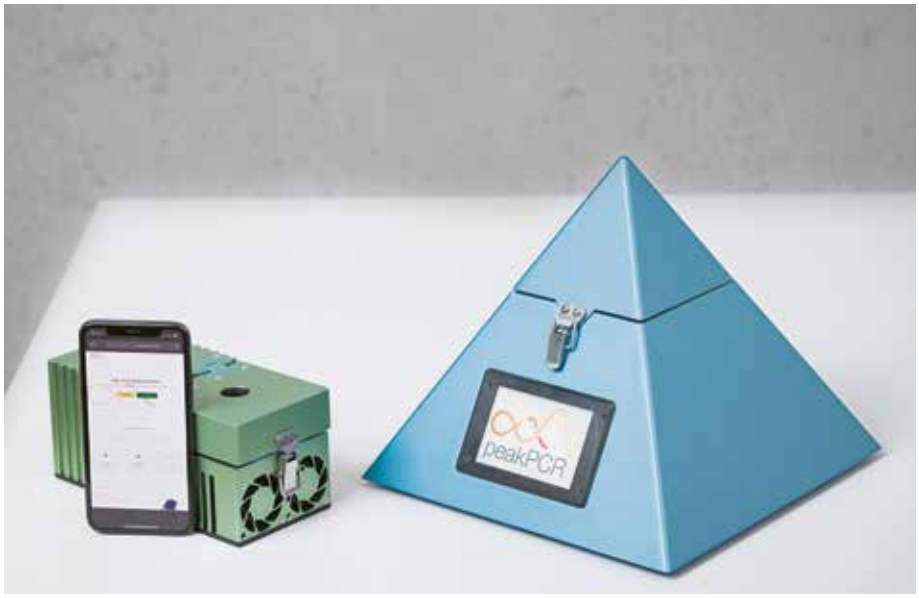
Collaborators: SolidarMed: Josephine Muhairwe. Radboud University Medical Center: Bram van Ginneken. FIND: Samuel Schumacher.

Image: Digital x-ray results from a patient's lung region. The software CAD-4COVID will use artificial intelligence algorithms to produce a heatmap (right) indicating regions of abnormality as well as a score (0–100) for suspicion of COVID-19. Credit: Radboud University Medical Center.

Investigators

Klaus Reither
Swiss TPH

Niklaus Labhardt
Swiss TPH



peakPCR: Making DNA Analyses Faster and More Accessible

Polymerase Chain Reaction (PCR) is a commonly used technique for amplifying and detecting DNA, and PCR-based testing has been widely adopted as a method of detecting SARS-CoV-2 infections. While this method is sensitive, it is currently slow and costly. To overcome these challenges, this project aims to develop a portable PCR device that will allow viral testing to be carried out more rapidly, at a lower cost and outside of high-tech environments. The device will have the potential to increase diagnostic capacity not only in high-income countries such as Switzerland, but also in low- and middle-income settings.

Collaborators: ETH Zurich: Michele Gregorini.

Image: Two designs for making PCR machines more accessible and portable. The devices can be controlled through a smartphone app. Credit: Kilian J Kessler.

Investigators

Wendelin Stark
ETH Zurich

High-Throughput Testing of SARS-CoV-2 Infection, Evolution and Immunity by Deep Sequencing

The global spread of COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has presented a public health crisis of a magnitude not experienced in over a century. A central challenge in mitigating the pandemic is the difficulty of detecting the viral infections and subsequently reducing transmission chains. This project aims to develop a high-throughput diagnostic method for detecting the virus along with a platform for detecting antibody-mediated immunity. This technology has the potential to scale quickly and broadly for possible population-level surveillance of the disease.

Image: Researchers work on high-throughput diagnostic methods.

Investigators

Sai Reddy
ETH Zurich

Yakir Guri
University Hospital Basel

Michael Nash
University of Basel

A Novel Rapid, Mobile, Lab-Independent and Sensitive SARS-CoV-2 Test at the Point-of-Need, to Break the Chain of Infection

Currently, diagnostic capacity to detect SARS-CoV-2 is centralized, requiring a complex workflow with highly trained staff, and the diagnostic tests themselves can be relatively inaccessible, slow to produce results and high in cost. Thus, this consortium seeks to fill an urgent unmet medical need for a mobile and rapid diagnostic test system for COVID-19 based on lateral flow assays. The project aims to provide a highly sensitive means of diagnosing SARS-CoV-2 infection at the point of need.

Collaborators: University Hospital Basel: Noé Brasier. SuSoS AG: Samuele Tosatti. Konplan Systemhaus AG: Oliver Weingart.

Image: A rapid point-of-need diagnostic test shows a lateral flow assay. A sample is loaded onto the sample pad (left) of the lateral flow assay. The sample then moves along the strip, where the viral proteins are immobilized and labeled. The readout device (right) then accurately quantifies the labeled proteins and displays the result. Credit: Alexander Tanno.

Investigators

Janos Vörös
ETH Zurich

Michael Osthoff
University Hospital Basel

DAVINCI: Development and Validation of a Lateral Flow Test to Detect COVID-19 Antigens and Immunity in Saliva

The COVID-19 pandemic has led to shutdowns and the home isolation of more than half of the world's population, resulting in severe economic impact. This research project addresses the current crucial need to develop an innovative, easy-to-use diagnostic test designed for consumers at home which addresses all relevant diagnostic questions for COVID-19 in a single test device. Specifically, the project aims to develop and validate a disposable rapid test device to detect SARS-CoV2 antigens and antibodies in saliva samples within 15 minutes.

Collaborators: Swiss TPH: Frank Dieterle. FHNW: Peter Spies. CSEM: Samantha Paoletti. HEMEX: Vanja Ivancevic, Pascal Winnen. BioInitials: Saso Jezernik. Effectum Medical: Nila-Pia Rähle.

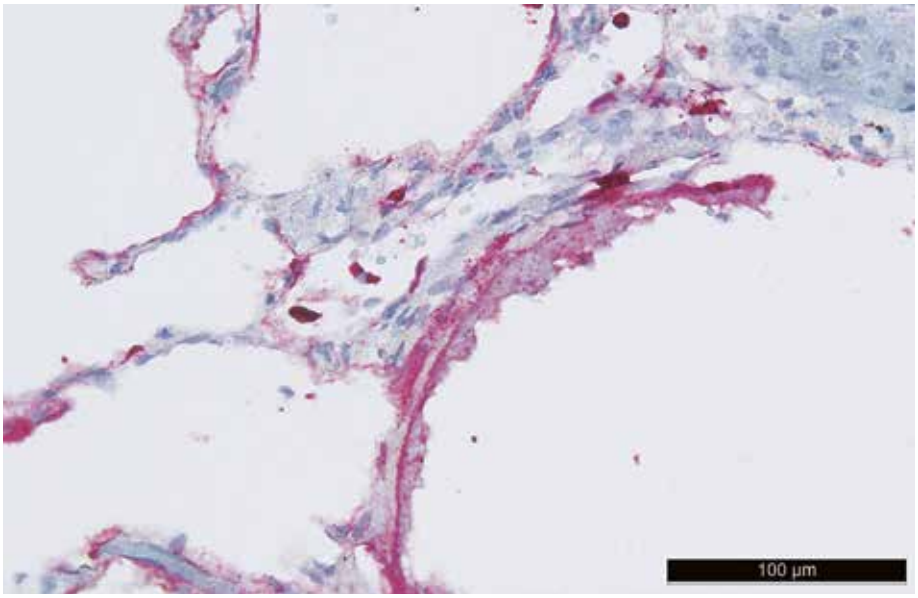
Image: The project aims to develop and validate a disposable rapid test device to detect SARS-CoV-2 antigens and antibodies in saliva samples within 15 minutes. Credit: DAVINCI.

Investigators

Daniel Paris
Swiss TPH

Daniel Richards
ETH Zurich

Stefan Stübinger
University of Basel



Lessons from the Deceased to the Living and Back: Investigation of SARS-CoV-2 Interactions with Human Cells, Tissues and Organs in a Unique Basel-Region Cohort of Autoptically Examined COVID-19 Patients

Very little is known about the pathobiology of COVID-19, its effects on human tissues, the spread of SARS-CoV-2 in the human body and its interactions with the immune system. This consortium will investigate *in situ* the interactions of SARS-CoV-2 with tissues and organs derived from deceased patients and patients suffering from severe COVID-19. The project will contribute valuable insights into the pathogenesis of COVID-19 and the future design of medical interventions for this disease.

Collaborators: University Hospital Basel: Stephan Frank, Thomas Menter, Lukas Bubendorf, Spasenija Savic, Jasmin Dionne Haslbauer, Ethan Taub, Johanna Lieb. Stanford University: Garry Nolan, David McIlwain, Sizun Jiang, Christian Schürch.

Image: SARS-CoV-2 antigens in the alveolar wall with a particular accentuation at the basal part of alveolar lining cells and in one capillary (upper right at 1 pm) as well as in isolated desquamated macrophages (intensively staining single cells). Credit: Alexandar Tzankov, Institute of Pathology, University Hospital Basel.

Investigators

Alexandar Tzankov
University Hospital Basel

Matthias Matter
University Hospital Basel

Gregor Hutter
University Hospital Basel

Stefano Bassetti
University Hospital Basel

Jürgen Hench
University Hospital Basel

Kirsten Mertz
University Hospital Basel

Hans Pargger
University Hospital Basel

Identification, Characterization and Optimization of High-Affinity Antibodies against SARS-CoV-2

There is a clear unmet need for novel anti-viral therapeutic approaches for treating COVID-19. To build protection against infections, the human body's immune system has both innate and adaptive strategies. Within our adaptive immune system, cells produce a repertoire of antibodies that can recognize, bind and neutralize infectious pathogens. This project aims to identify high-affinity protective antibodies generated in COVID-19 patients which as such are specific to SARS-CoV-2 and could be further harnessed for therapeutic interventions.

Collaborators: ETH Zurich: Randall Platt.

Image: A multi-pipetter quickly delivers equal measures into sample wells.

Investigators

Andreas Moor
ETH Zurich

Yakir Guri
University Hospital Basel

ISINC-19: Immune Senescence in COVID-19

It is still unclear why some individuals infected with SARS-CoV-2 develop severe illness whereas others develop only mild or even no symptoms. This research consortium aims to investigate the role of immune system dysfunction in COVID-19 clinical presentation. The team will explore how biological processes in immune cells, particularly metabolism, and their respective functions are affected in patients with differing levels of disease severity with the aim of improving therapeutic interventions for COVID-19 patients.

Collaborators: University Hospital Basel: Daiana Stolz.

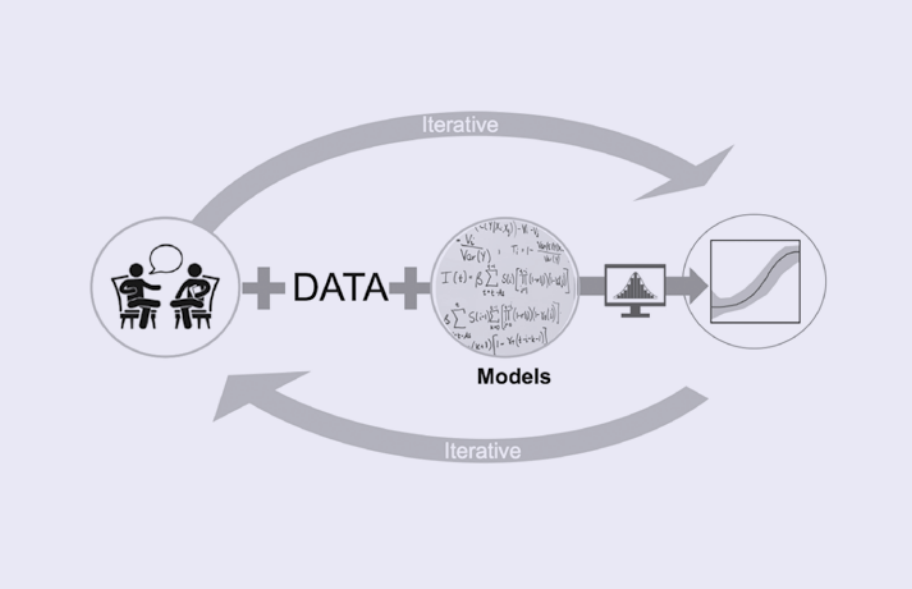
Image: A researcher performs flow cytometry using the Cytek Aurora. Credit: C. Berger.

Investigators

Christoph Hess
University of Basel & University of Cambridge

Glenn Bantug
University of Basel

Christoph Berger
University Hospital Basel



Using Model-Based Evidence to Optimise Medical Intervention Profiles and Disease Management Strategies for COVID-19 Control

One of the challenges presented during the COVID-19 pandemic is how to design interventions and deployment strategies to maximize potential impact. This consortium seeks to harness mathematical modelling and machine learning approaches using available information on disease dynamics and intervention characteristics. The project aims to provide model-based translational evidence to guide and optimize COVID-19 strategies for diagnostics, therapeutic interventions, disease surveillance and management.

Collaborators: Swiss TPH: Monica Golumbeanu, Andrew Shattock.

Image: Modelling support is an iterative process that uses available data to generate predictions for decision making. Mathematical modelling can help with prioritization and investment in novel medical tools for COVID-19. Credit: Melissa Penny.

Investigators

Melissa Penny
Swiss TPH

Nakul Chitnis
Swiss TPH

Roland Regoes
ETH Zurich

COVent: Improve Ventilation Safety by Means of Intra-Tracheal Pressure Monitoring – A Short-Term Solution

Part of the therapeutic strategy for critically ill COVID-19 patients is mechanical ventilation support. However, ventilators are in short supply around the world and there are safety concerns related to low-cost, do-it-yourself ventilators. In addition, there is a risk of ventilator-induced lung injury from excessive pressure. This consortium will critically evaluate a range of available ventilators and integrate innovative pressure sensors into low-cost ventilators to improve patient care and outcomes and help to overcome the global ventilator shortage.

Collaborators: CSEM: Sören Fricke.

Image: Researchers measure pathophysiological lung parameters in a lung simulator ventilated by a low-cost ventilator. Pressure measurements, visualized on the computer screen, enable safety assessment of the low-cost ventilator. Credit: Kiran Kuruvithadam.

Investigators

Thomas Erb
University Children's Hospital Basel

Jürg Hammer
University Children's Hospital Basel

Mirko Meboldt
ETH Zurich

Marianne Schmid Daners
ETH Zurich

Target Discovery and Rational Design of Therapeutics against SARS-CoV-2

Investigators

Randall Platt
ETH Zurich

Despite intense research into SARS-CoV-2 infection and its implications for our health, we are still lacking effective treatments that specifically target this deadly virus. Therefore, optimal therapeutic strategies for patients with COVID-19 are urgently needed. This project will harness CRISPR-based technologies to identify factors that are crucial for SARS-CoV-2 to infect and cause disease in humans. In this way, the project aims to reveal novel therapeutic strategies for COVID-19 patients in the future.

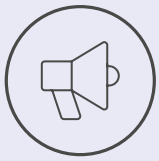
Image: A researcher uses an imager to examine results from a gel electrophoresis assay.

The BRCCH enables outstanding and innovative paediatric research to address unmet clinical needs, to develop and improve diagnostic tools and to design novel interventions for young people. Here, a researcher examines samples in a high-powered imaging microscope as part of a research project that aims to bioengineer the microbiota.

BRCCH Output

Researchers and clinicians involved in BRCCH research have been very productive since the Centre's launch. The BRCCH commends our researchers for their scientific output and research dissemination activities:

15 published papers to date, with 15 more in the pipeline



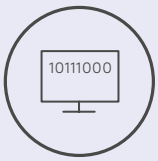
9 research disseminations in the news and media via coverage formats such as interviews, podcasts and articles

1 patent application submitted by the "Precision Microbiota Engineering for Child Health" consortium

10 capacity-building events and initiatives involving BRCCH-funded researchers

2 contributions to technical reports on COVID-19 modelling projections to the European Centre for Disease Prevention and Control

30 research presentations (talks and posters) by researchers on BRCCH-funded work



2 sets of code and data published open access relating to the modelling work of the "Using Model-Based Evidence to Optimise Medical Intervention Profiles and Disease Management Strategies for COVID-19 Control" consortium

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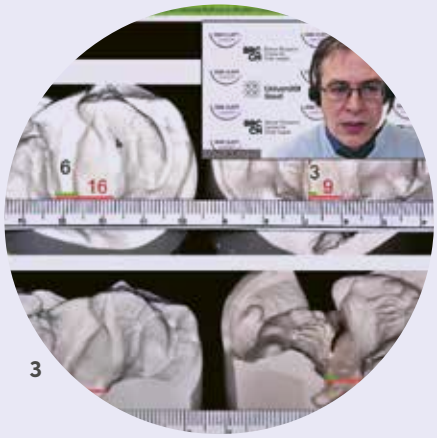
2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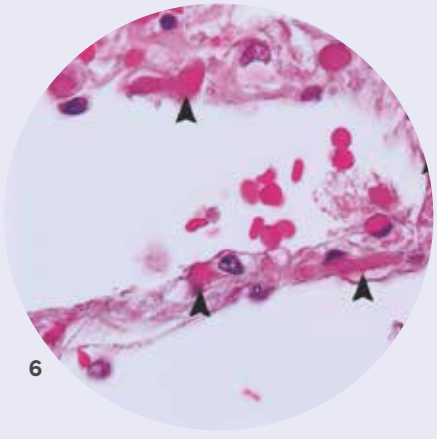
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Credit: 1–2. SolidarMed and Swiss TPH; 3. BRCCH; 4. Beda Brun del Re; 5. Dr R Nienhold, Cantonal Hospital Baselland, Liestal; 6. Ackermann et al. 2020 NEJM.

Select Highlights:

MistraL: Mitigation Strategies for Communities with COVID-19 Transmission in Lesotho Using Artificial Intelligence on Chest X-Rays and Novel Rapid Diagnostic Tests

1. A mobile x-ray unit stands ready to travel to various locations in the districts of Lesotho as part of the research carried out by the MistraL consortium.
2. Two healthcare workers are training to use x-ray equipment.

Burden-Reduced Cleft Lip and Palate Care and Healing

3. Along with international colleagues, Dr Andreas Mueller and additional consortium members led a two-day training webinar related to the one-step unilateral cleft lip and palate surgery method, with approximately 1100 virtual attendees.
4. Dr Barbara Solenthaler did science outreach as a guest star at two Pestalozzi Schoolcamps aimed at Swiss primary school classes, where she engaged 90+ students with lectures and hands-on workshops on computer science.

Lessons from the Deceased to the Living and Back: Investigation of SARS-CoV-2 Interactions with Human Cells, Tissues and Organs in a Unique Basel-Region Cohort of Autoptically Examined COVID-19 Patients

5. Prof Kirsten Mertz was interviewed by Prime News about her research on the pathobiology of COVID-19 for an article titled "There Are Still Many Open Questions about Corona."
6. A figure from a highly cited paper by Prof Alexandar Tzankov and colleagues entitled "Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19" in the *New England Journal of Medicine*.[3] This is one of the many papers by members of the consortium on the pathoimmunology of COVID-19.

Governance

The BRCCH's strategy and activities are governed by the BRCCH Board, which is formed of representatives from the University of Basel and ETH Zurich. The BRCCH academic leadership, Director Prof Georg Holländer and Vice Director Prof Sai Reddy, is responsible for its operations, including the shaping of the Centre's research strategy and its implementation. The Strategic Scientific Advisory Board (SSAB), comprising national and international experts, advises the Directors and the Board based upon its members' extensive collective expertise. An *ad hoc* Project Evaluation Board (PEB) is responsible for the independent scientific evaluation of research applications.

BRCCH Board

Prof Andrea Schenker-Wicki
Chair of BRCCH Board
President
University of Basel

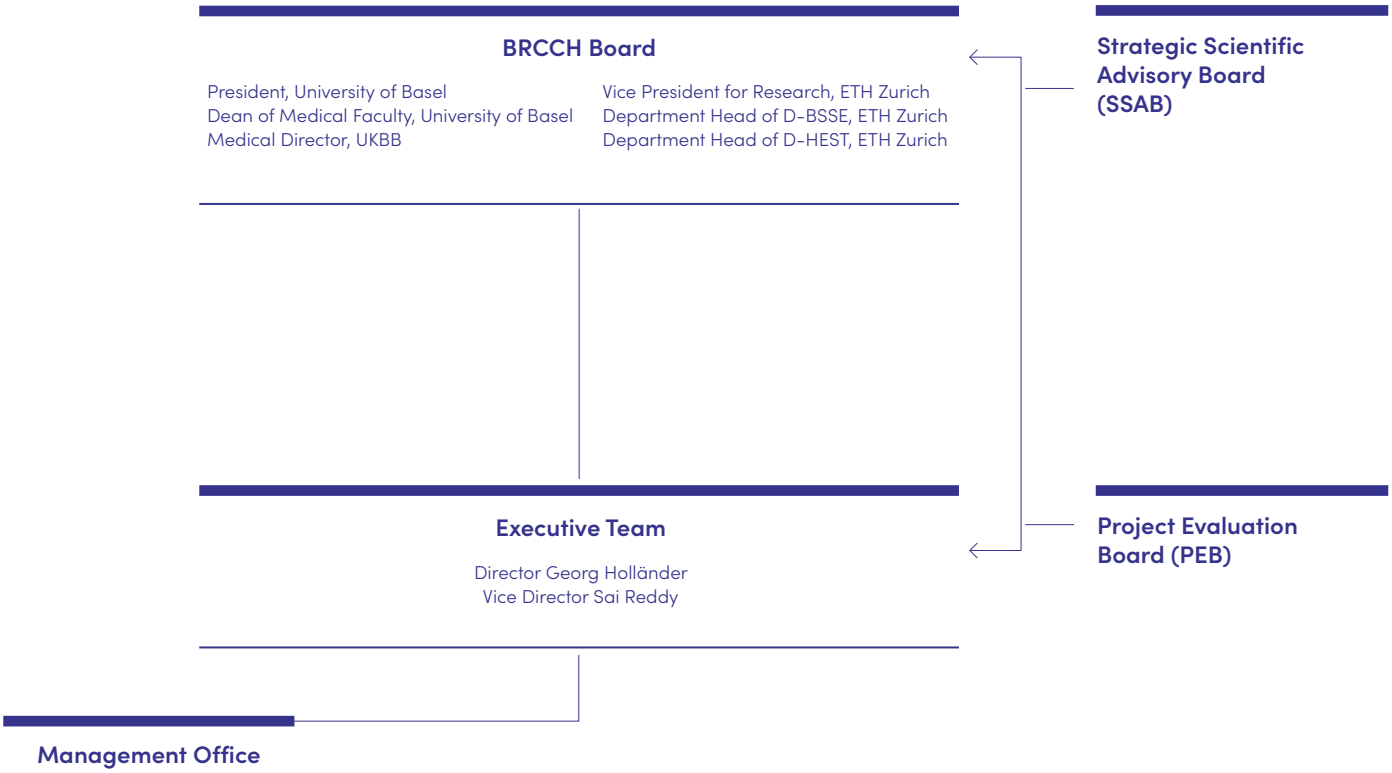
Prof Detlef Günther
Co-Chair of BRCCH Board
Vice President for Research
and Corporate Relations
ETH Zurich

Prof Primo Schär
Dean of Medical Faculty
University of Basel

Prof Niko Beerenwinkel
Department Head of D-BSSE
ETH Zurich

Prof Urs Frey
Medical Director
University Children's Hospital Basel

Prof Stephen Ferguson
Department Head of D-HEST
ETH Zurich



Finance

The BRCCH benefits from a generous donation by Fondation Botnar of CHF 100 Mio, which will support its activities from 2019 to 2028. This budget is equally shared between the University of Basel and ETH Zurich. This financing has allowed the BRCCH to establish a research project portfolio currently comprising the Multi-Investigator Programme and the Postdoctoral Excellence Programme. In spring 2020, the BRCCH further benefited from an additional CHF 15 Mio from Fondation Botnar to provide rapid support to research consortia aiming to mitigate the effects of the COVID-19 pandemic. The Centre's next steps include the launch of the Principal Investigator Initiative and the continuation of plans for up to six assistant professorships to be initially supported by the BRCCH.

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1. Institute for Health Metrics and Evaluation (IHME). GBD Compare Data Visualization. Seattle, WA: IHME, University of Washington, 2018. Available from http://vizhub.healthdata.org/gbd-compare. (Accessed 20.10.2020.)

2. Burstein R, Henry NJ, Collison ML, et al. 2019. Mapping 123 million neonatal, infant and child deaths between 2000 and 2017. Nature 574, 353–358. https://doi.org/10.1038/s41586-019-1545-0. Figure reproduced under the permission of the Creative Commons Attribution 4.0 (http://creativecommons.org/licenses/by/4.0/). Changes to the figure: the overlay of BRCCH collaborators and partners onto map and the filtering of the colour tones.

3. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, Vanstapel A, Werlein C, Stark H, Tzankov A, Li WW, Li VW, Mentzer SJ, and Jonigk D. 2020. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. New England Journal of Medicine 383:120–28. doi: 10.1056/nejmoa2015432.

Impressum
Publisher: Botnar Research Centre for Child Health
Editor: Maressa Takahashi
Proofing: Katharine Handel
Design: STUDIO NEO, Basel
Print: Steudler Press AG
Print run: 400 copies

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