BRC CH Botnar Research Centre for Child Health

Annual Report 2021
Botnar Research Centre for Child Health

University of Basel ETH zürich

Supported by Fondation Botnar

Facts and Numbers 2021

Jan 1, 2019
Start of Operations

4
Partner Institutions

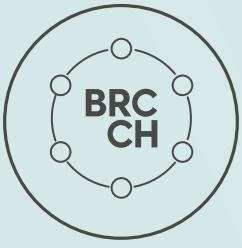
22
International Research Collaborations

47
Project Investigators

32.6
Mio CHF in Research Project Support

23
Research Projects

36
Scientific Outputs



4
Research Programmes Launched

Over the course of the past decades, there has been impressive progress in improving the health of young people. Children under five years of age are especially vulnerable to infectious diseases, including most prominently malaria, pneumonia and diarrhoea. Health inequalities and challenges in access to healthcare constitute an additional threat to young people in low- and middle-income countries.

Much of this burden can be alleviated with appropriate preventive measures, robust diagnostics and adequate therapies. The development and implementation of new, cost-effective and sustainable healthcare solutions for those most in need are fundamental for improving the next generation's quality of life. For this to become a reality, innovative biomedical tools and digital health technologies will need to be employed in order to address unmet medical needs. The Botnar Research Centre for Child Health, in partnership with the University of Basel and ETH Zurich, focus its efforts on developing efficient and effective interventions and treatments for the most vulnerable worldwide.

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An embryoid body is a mass of human embryonic stem cells forming a 3D structure. These embryoid bodies are useful models for studying the development and formation of specific organs, as well as for modelling human diseases and potential therapeutic approaches. Credit: Nissim Benvenisty Lab, Azrieli Center for Stem Cells and Genetic Research, Hebrew University of Jerusalem.

Dear colleagues and friends of the BRCCH,

Prof Georg Holländer
Director

Prof Sai Reddy
Vice Director

Since the beginning of its operations three years ago, the BRCCH has worked closely with its partners, the University of Basel, ETH Zurich, University Children's Hospital Basel (UKBB) and the Swiss Tropical and Public Health Institute (Swiss TPH), along with researchers around the world in order to drive outstanding and innovative paediatric research.

The course of the pandemic over the last two years has provided the BRCCH with additional challenges to meeting its remit. Nonetheless, through its Fast Track Call, the Centre has been able to initiate eleven research projects that are contributing to COVID-19-related research and public health in the domains of diagnostics, immunology and medical interventions. For example, researchers at the BRCCH's partner institutions have successfully identified a new biomarker for COVID-19 severity, developed methods for more comprehensive genomic surveillance and innovated rapid diagnostics for past and current infections. At the beginning of the year, a collaboration with the European & Developing Countries Clinical Trials Partnership secured additional research collaborations dedicated to improving the surveillance and management of COVID-19 in sub-Saharan Africa. The progress of these activities was widely shared during a webinar on the future of COVID-19 research. With the participation of national and international experts, a roadmap was charted for COVID-19-related research in immunology, epidemiology and bioengineering.

In 2021, the BRCCH also expanded its research portfolio: a call for new research projects was launched and a programme was inaugurated that both supports early career researchers in each of our partner institutions and also fosters interaction among these promising scientists. At the close of the year, we launched a call for proposals for the Principal Investigator Initiative, which supports interdisciplinary research in global paediatric health and medicine.

Over the past year, an external Evaluation Committee reviewed the BRCCH's research programmes and identified how best to meet the Centre's goals. The report's conclusions were widely shared with our stakeholders, whose support we greatly appreciate.

We are pleased to present here a summary of the Centre's 2021 research activities. We sincerely thank all BRCCH researchers and their teams at our partner institutions and elsewhere around the world for their engagement in improving the health and well-being of young people. We also wish to express our enormous gratitude to Fondation Botnar for their continued support of the BRCCH.

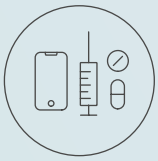
With our best wishes,

Georg Holländer

Sai Reddy

A Hub for Paediatric Research

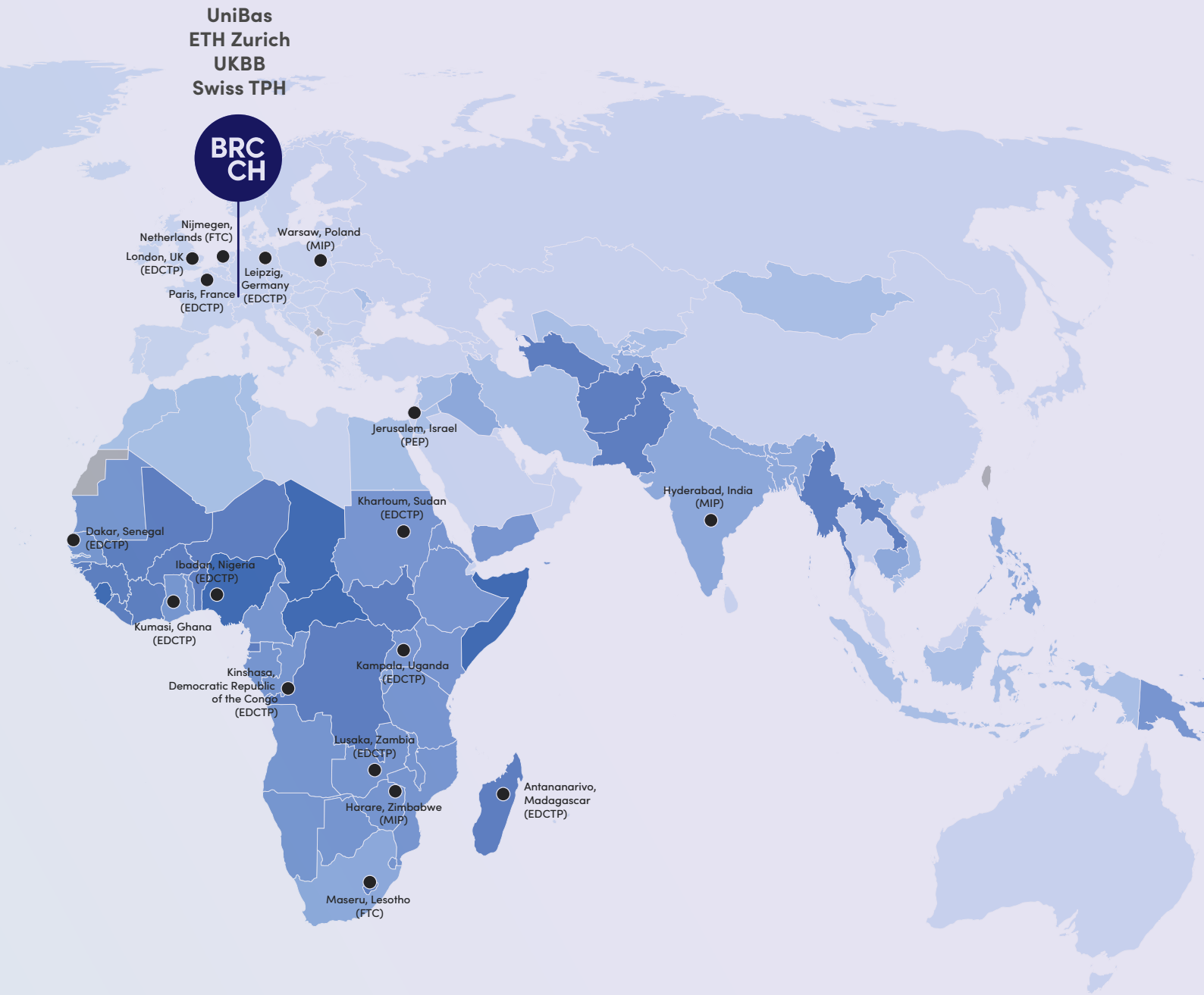
The BRCCH is located in Basel, Switzerland, and is generously supported by Fondation Botnar. We maintain close ties with researchers at our four partner institutions: the University of Basel, ETH Zurich, University Children's Hospital Basel and the Swiss Tropical and Public Health Institute. In addition,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



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 to foster a research community that is able to develop new healthcare solutions for the benefit of young people worldwide. To make this happen, medical teams 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.

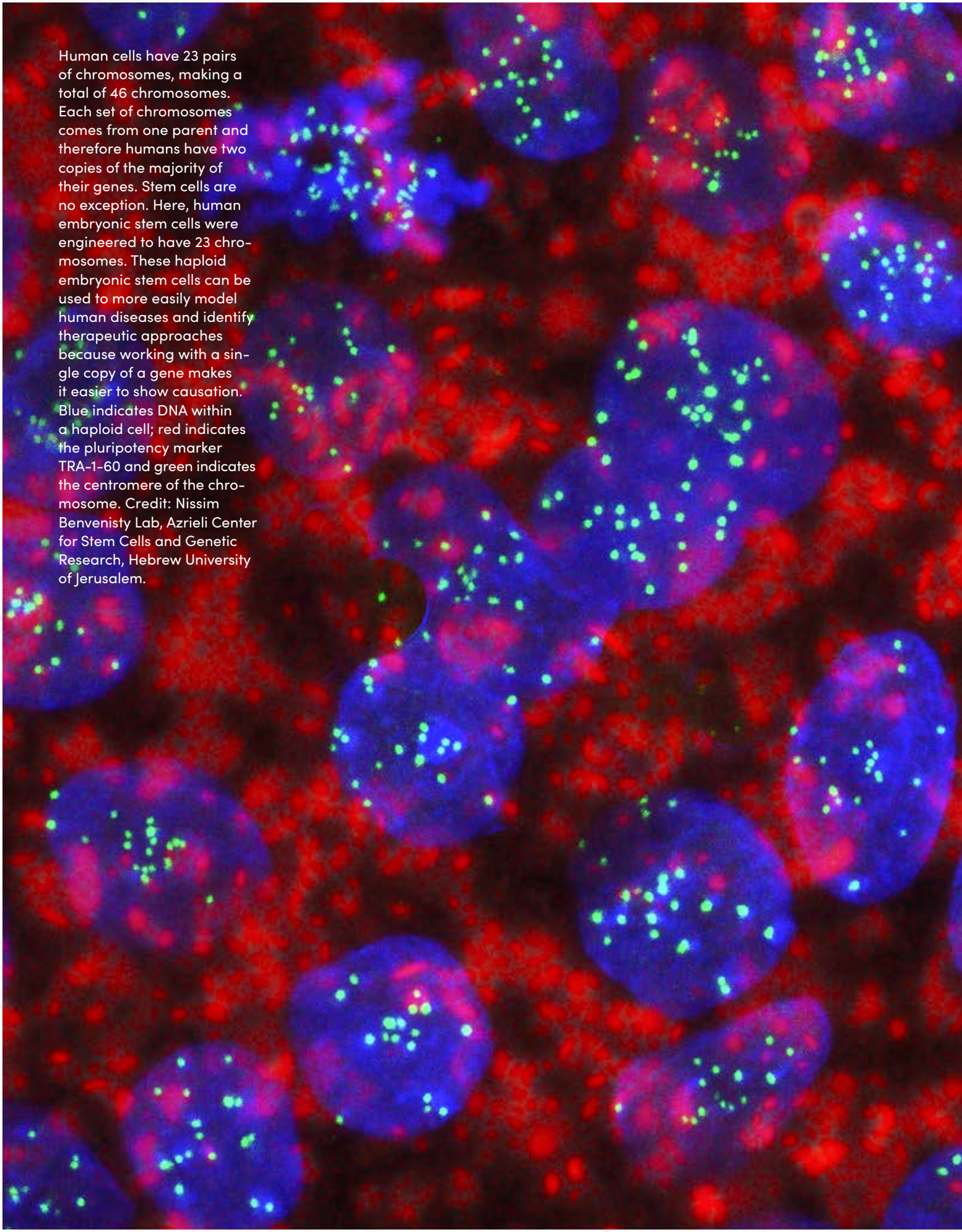
Our Vision
is to create a centre that fosters multidisciplinary and translational research in order to address unmet medical needs in paediatric health. The objectives are to create novel solutions for the prevention, diagnosis and treatment of disease and to develop tools that can accurately predict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



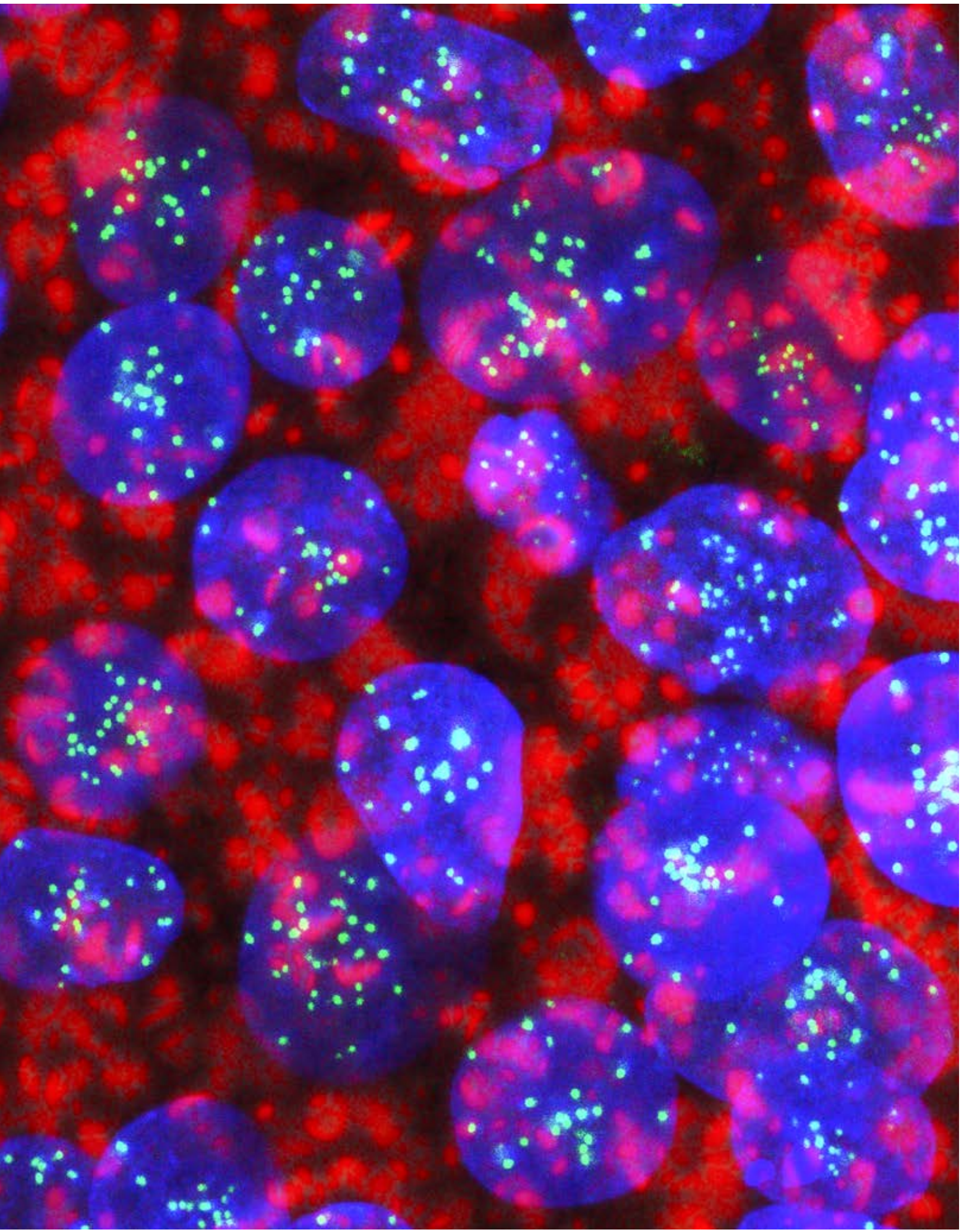
BRCCH collaborators and partners involved in:
MIP: Multi-Investigator Programme
FTC: Fast Track Call
PEP: Postdoctoral Excellence Programme
EDCTP Collaboration: European and Developing Countries Clinical Trials Partnership
(as of December 2021)

Total under-five mortality rate (deaths per 1000 live births)[1]

- 0–12
- 12–25
- 25–40
- 40–75
- 75–100
- 100–150
- No data



Human cells have 23 pairs of chromosomes, making a total of 46 chromosomes. Each set of chromosomes comes from one parent and therefore humans have two copies of the majority of their genes. Stem cells are no exception. Here, human embryonic stem cells were engineered to have 23 chromosomes. These haploid embryonic stem cells can be used to more easily model human diseases and identify therapeutic approaches because working with a single copy of a gene makes it easier to show causation. Blue indicates DNA within a haploid cell; red indicates the pluripotency marker TRA-1-60 and green indicates the centromere of the chromosome. Credit: Nissim Benvenisty Lab, Azrieli Center for Stem Cells and Genetic Research, Hebrew University of Jerusalem.



2021 in Review

February
BRCCH and EDCTP Joint Initiative

The BRCCH and the European & Developing Countries Clinical Trials Partnership (EDCTP) partnered on a new joint initiative to support multi-national collaborations for research to mitigate COVID-19. The three projects focus on immunology, diagnostics and health screening strategies for COVID-19 in low- and middle-income country (LMIC) settings. The projects were launched in January 2021 and will run for two years. BRCCH researchers are based at ETH Zurich, Swiss TPH and University Hospital Basel, while participating EDCTP researchers are based at 15 institutions located around the world. In total, 31 investigators are involved across the three projects. You can read about the projects on pages 35–37. Credit: SolidarMed and Swiss TPH.

April
BRCCH Evaluation

In spring 2021, the BRCCH underwent its first evaluation by external experts. The process was conducted by an external Evaluation Committee made up of six experts, whose expertise spans the BRCCH's mandate, and it was chaired by Prof Susan Gasser (Director of Fondation ISREC). The Evaluation Committee was tasked with performing an in-depth retrospective and prospective assessment of the Centre across four key areas: 1) Vision and Strategy; 2) Global Translation; 3) Organization and Governance; and 4) Sustainability. The final report concluded that the BRCCH and its stakeholders are successfully working towards improving the health and well-being of children and adolescents worldwide, particularly in LMICs. This is enabled by cross-institutional efforts dedicated to internationally competitive and innovative projects. In addition, the Centre's efforts in research operations, communications and community-building were recognized as a particularly strong aspect of its work.

The Evaluation Committee's report was presented to and discussed with the BRCCH's Supervisory and Advisory Committees, along with Fondation Botnar. The Centre's future efforts will be guided by the findings of this report and it will further shape the BRCCH's programme going forward.

May
BRCCH Research Building

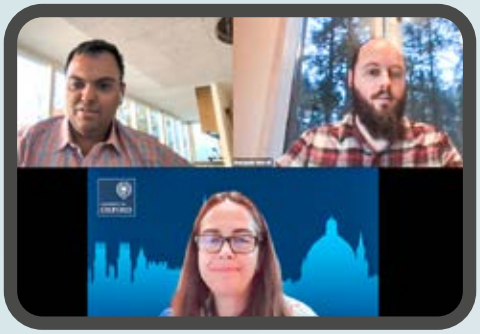
The Canton Basel-Stadt announced plans to construct a new research building on the corner of Spitalstrasse and Schanzenstrasse and held an architectural competition for its design. Among the 48 entries, the jury unanimously selected the project submitted by Guerra Clauss Garin Architekten (Basel). The winning design, entitled "R2-D2," convinced the judges with its progressive solutions for constructing, operating and maintaining a sustainable research building with a low carbon footprint. The building is scheduled to be completed by 2025. Several of the BRCCH's research groups will call this new building their home.

July
Launch of Post-doctoral Excellence Programme

The BRCCH launched five new research projects as part of its Postdoctoral Excellence Programme (PEP) initiative. This programme aims to foster the next generation of scientific leaders who will pursue interdisciplinary and step-changing research in order to address critical unmet needs and challenges in global paediatric health. Fellows Dr Kanika Dheman (ETH Zurich), Dr Keith Gunapala (University of Basel), Dr Nicole Zoratto (ETH Zurich), Dr Gillian Levine (Swiss TPH) and Dr Sarah Brüningk (ETH Zurich) are conducting projects ranging in topic from novel devices for paediatric blood sampling to novel therapies for inherited diseases and digital tools for improving paediatric medicine. Together with established hosting Principal Investigators and Collaborators, these PEP Fellows will implement highly translational and ambitious research proposals over the next three years. You can read about the projects on pages 38–43.

August
Launch of Principal Investigator Initiative

The BRCCH opened a call for applications for research projects for its new Principal Investigator Initiative (PII). The PII aims to drive interdisciplinary research that addresses critical challenges in global paediatric health and medicine. The call sought translational research projects that will deliver novel innovations across paediatric diagnosis, disease treatment and prevention. It also welcomed projects that aim to advance the implementation and uptake of step-changing paediatric health interventions, particularly in LMICs. PII projects are intended to be four years in duration, with up to 1 Mio CHF in funding per award. The projects that are selected for funding will start in summer 2022.



October
Future of COVID-19 Research Webinar

A webinar on the future of COVID-19 research highlighted significant research progress and the roadmap ahead for COVID-19 research related to immunology, epidemiology and bioengineering. Prof Teresa Lambe OBE (University of Oxford) reviewed the development of the Oxford/AstraZeneca anti-SARS-CoV-2 vaccine. Prof Benjamin Murrell (Karolinska Institutet) discussed the challenges of finding neutralizing antibodies for SARS-CoV-2 variants. Finally, Prof Sai Reddy (ETH Zurich and BRCCH) presented his latest work on COVID-19 genomic surveillance and new viral variant prediction. The event, which was attended by over 130 people, was a wonderful moment of science and stimulated lively discussion, and it attracted interest from around the world with participants from 30 countries including China, Zimbabwe, Nepal and Ethiopia.

"Thanks a lot for this very interesting course, which was a very different angle to communication workshops that I have previously attended!"

"I think this course really raised my awareness of very different cultural styles of communication, and I hope to put some of the advice we were given into action in my future communication."

October
Launch of Early Career Programme

The BRCCH's vision is to develop a community of paediatric researchers interested in developing innovations that can ideally be implemented in both the Global North and South. To this end, the BRCCH is developing an in-house initiative that enables early career researchers to gain know-how suitable for the Centre's mandate that complements existing structured postgraduate programmes available at the University of Basel and ETH Zurich. The Centre's Early Career Programme (ECP) will cover the following core elements: Education, Network and Community Building, and Professional Development. The first workshop on how to communicate effectively in multicultural settings took place online and was led by Mark Moser (University of Applied Sciences and Arts Northwestern Switzerland FHNW), with the participation of early career researchers involved in BRCCH-funded projects.

November
Treffpunkt Science City

Treffpunkt Science City in Zurich is an annual public science event hosted by ETH Zurich. This year's theme addressed the subject of "Rich and Poor" through presentations, exhibition booths, lab visits and panel discussions. This public engagement event designed for all ages ran for several days throughout October and November. BRCCH MIP investigator Prof Emma Slack gave a lecture entitled "A Pill against E.coli bacteria?". Her recorded presentation has gained 1875 views online to date. BRCCH MIP investigators Dr Andreas Mueller and Dr Barbara Solenthaler and their teams exhibited the prototype of a palatal orthopaedic plate fabricated via 3D printing, which is used in clinics for cleft lip and palate repair. BRCCH FTC investigator Prof Wendelin Stark and his team showcased their *peakPCR* device which allows rapid, simple and low-cost diagnostic testing for SARS-CoV-2. This year, the event welcomed over 4500 visitors of all ages.

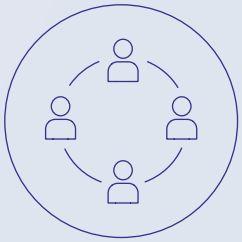
December Image Contest

This December, early career researchers submitted images from their BRCCH-supported research to the first edition of the BRCCH Image Contest. Three winners were selected by the BRCCH Directors.

- Dr Keith Gunapala (PEP fellow) – his image represents haploid embryonic stem cells and can be seen on pages 6–7.
- Dr Michele Gregorini (FTC COVID-19 researcher) – in his image, BRCCH researchers are developing an innovative PCR device in resource-limited settings. The image can be seen on page 24.
- Ronja Rappold (MIP researcher) – her image (above) shows a cross-section of mouse caecal tissue including food content. It has been stained with hematoxylin and eosin to reveal the nuclei and the extracellular matrix respectively. Researchers use these stainings to assess the pathological state of tissues.

The prize winners will be awarded with sponsorship to participate in a scientific congress of their choice.

Here is what to look forward to in 2022



Community
BRCCH Seminar Series
The BRCCH seminar series aims to showcase the BRCCH research programme and to highlight cutting-edge science in paediatrics. Each seminar will feature a presentation by a BRCCH Investigator followed by an invited external guest speaker and each seminar will focus on a theme linked to the Centre's research scope. Accompanying informal networking events will help to forge relationships within the BRCCH community. The BRCCH is looking forward to welcoming its community at these seminars once more.

Early Career Programme
The BRCCH has established an Early Career Programme (ECP), a programme encouraging promising young BRCCH researchers to become independent scientists. The ECP provides the opportunity to gain new know-how during interactive workshops and establish a wide network. From 2022 onwards and if COVID-19-related public health measures allow, we aim for the lectures to take place in person in Basel. Future lectures will be given by Dr Fabian Käser (Commission for Research Partnerships with Developing Countries (KFPE)) and Jonas Karlström (UNICEF) to discuss how to establish fair and equitable global research partnerships and by Prof Yvonne Maldonado (Stanford University) on the topic of unmet needs in global paediatric health.

Research
Principal Investigator Initiative
The Principal Investigator Initiative (PII) is one of four BRCCH funding programmes and encourages collaborative efforts with BRCCH partner institutions, in particular projects with a clear path for translation in LMICs. Project proposals are evaluated by an international expert review panel. Each approved project will receive up to 1 Mio CHF and will run for a period of four years starting in 2022. The BRCCH looks forward to announcing the successful applicants in spring 2022.

Assistant Professorships
Over the coming years, the BRCCH aims to create up to six professorships at the University of Basel and ETH Zurich. The research foci of these posts will relate to scientific domains relevant to the BRCCH's mission. Plans are well advanced to establish positions in Paediatric Digital Health Data and Analytics, Engineering Biomolecular Systems for Diagnostics, and Ethics and Policy in Paediatric Digital Health.

i) The professorship in Paediatric Digital Health Data and Analytics is expected to create innovative tools and technologies that will enable the use of multimodal paediatric health-related data. Given the significant global traction around digital health research and technologies, a strategic position will be created within the fields of computational medicine and paediatric digital health that will allow the Centre and its partner institutions to become more competitive and increase their ability to advance research in these important domains.

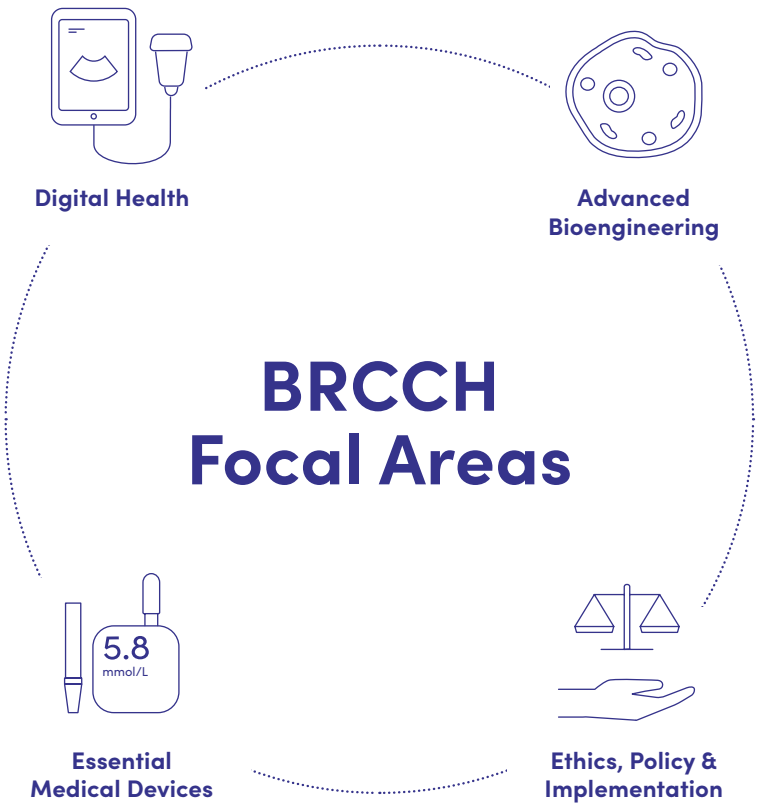
ii) The professorship in Engineering Biomolecular Systems for Diagnostics is tasked with advancing novel and innovative approaches in biomolecular diagnostics that support sophisticated point-of-care diagnostic systems suitable for use in resource-limited settings. With this new professorship, the BRCCH will be supporting technology-focused research that complements existing activities within our partner institutions and adds additional expertise in the clinical application of engineered biological systems.

iii) The professorship in Ethics and Policy in Paediatric Digital Health will address ethical and policy challenges in paediatric health and medicine in the digital era. The professorship is expected to generate highly valuable knowledge that will influence ethical standards, regulatory frameworks and policies surrounding the development, use and implementation of digital health technologies and data in the paediatric population – now and in the future.

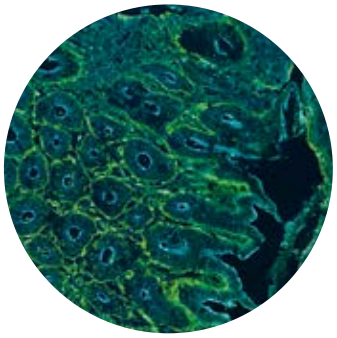
Research building
In 2025, the BRCCH will move into a new research building, which is located next to the *Schällemätteli* Basel life sciences campus. The building will be home to five BRCCH research groups, all of which will focus on innovative *in silico* science relevant to the Centre's scope. The building is strategically well placed, adjacent to the Department of Biosystems Science and Engineering (ETH Zurich), University Children's Hospital Basel and the University of Basel. Bringing BRCCH research groups together under one roof will further foster trans-disciplinary and inter-institutional collaborations, which constitutes one of the Centre's principal aims.

Strategy

The BRCCH and its partners conduct multidisciplinary research projects that address unmet medical needs in the context of a wide range of communicable and non-communicable medical conditions in young people. These efforts focus on diseases that cause a significant burden to individuals, their families and the wider community, irrespective of an individual's societal conditions. The BRCCH's research goals are to prevent, mitigate and where possible cure diseases and therefore focus on improving the health of young people. There are four broad research areas at the centre of this effort.



Paediatric Digital Health
Age-specific solutions in computational and digital medicine are particularly rare for young people. Using digital tools specifically tailored to the needs of children and adolescents, the BRCCH and its partners seek to collect high-quality, multi-modal data related to the health and disease states of individuals in these particular age groups. The collection of this data constitutes an essential step towards effective disease modelling, diagnosis, treatment and monitoring. A multi-pronged effort in digital health will fill current knowledge gaps and thus create opportunities for unique, valuable and impactful research in paediatric digital health.



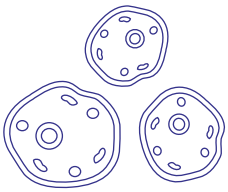
Advanced Bioengineering for Paediatric Medicine
Ground-breaking advances in bioengineering (biotechnology and computational biology) and biomedical research have resulted in a current era of improved precision in medicine, though these improvements have so far primarily been applied to diseases affecting adults. The BRCCH therefore aims to support bioengineering-based advances in precision medicine specific to paediatrics and to foster its application to health challenges in young people, especially those in LMICs. A personalized and disease-specific prevention and/or treatment will be possible in the future thanks to the availability of bio-engineering-enabled precision medicine. Credit: Ronja Rappold.

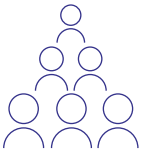
Essential Paediatric Medical Devices
The use of age-appropriate and age-effective medical devices is critical for reducing disease burden in young people. However, there is a generally acknowledged deficiency of medical devices that are specifically designed to be used in the paediatric age group due to the physiological differences between young people and adults. Moreover, this deficiency is further compounded for devices to be implemented in LMICs, since they have been primarily, if not exclusively, developed for use in high-income countries. The BRCCH supports the innovative design of essential medical devices that meet the criteria to be used both in young people and under conditions relevant to LMICs. Credit: ETH Zurich/Alessandro Della Bella.

Ethics, Policy and Implementation Research in Paediatric Health
The BRCCH wants young people across different societies to have broad access to innovative technology and digital health solutions, thus benefiting society at large and democratizing these essential tools for health. However, many technologies have been deployed without due ethical considerations or circumspect policies in place. Also, additional research is needed on how digital tools influence behavioural changes and decision-making in health issues that concern young people and their caregivers. The BRCCH therefore actively supports research dedicated to ethics, policy and implementation related to paediatric digital health interventions. Credit: Daniel Mäusezahl and Stella Hartinger Peña.

Research Portfolio

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



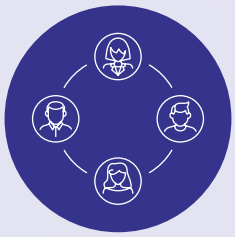


Cellular Systems — **Population**

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 LMICs. 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
Projects in this category are positioned on the path to implementation at a stage where previously generated 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 and/or therapy. The realization of these projects forms an essential element of the BRCCH's remit of translating and implementing findings from basic science.

Mature-Stage Research
These projects test the feasibility, robustness and usefulness of methods and medical devices for diagnosing, treating, monitoring and predicting the 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 in order 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.



Multi-Investigator Programme

The Multi-Investigator Programme (MIP) projects are essential cornerstones of the BRCCH's research portfolio. This programme forges the collaboration of multidisciplinary teams composed of research investigators from our four partner institutions and also fosters international collaborations that enhance the likelihood of clinical translation and implementation worldwide.

Four projects are currently being supported by the MIP initiative. They began their activities in early 2020 and will run for five years.

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

Overview: In many LMICs, 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 project will assess the efficacy and improve the performance of an interactive mobile phone-based application using 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: The consortium has successfully completed a five-month pilot study involving 176 families with the aim of testing and adapting the mobile phone-based application along with the survey tools. This study enabled the improvement of technical features, user content and in-app assessment of developmental milestones based on local feedback. The consortium has now launched a randomized controlled trial in which the digital tool will be further assessed for its impact, cost-effectiveness and scalability for improving child health and development in LMIC settings. They have also launched a scoping study to examine best practices in digital tech interventions for young children in LMICs.

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

Image: A healthcare worker visits a family in San Marcos in Peru as part of a home-visiting programme to support families with the early development of their children. Credit: Swiss-Peruvian Health Research Platform/Digital Support Systems to Improve Child Health and Development.

Lead Researchers

Günther Fink
Swiss TPH

Daniel Mäusezahl
Swiss TPH

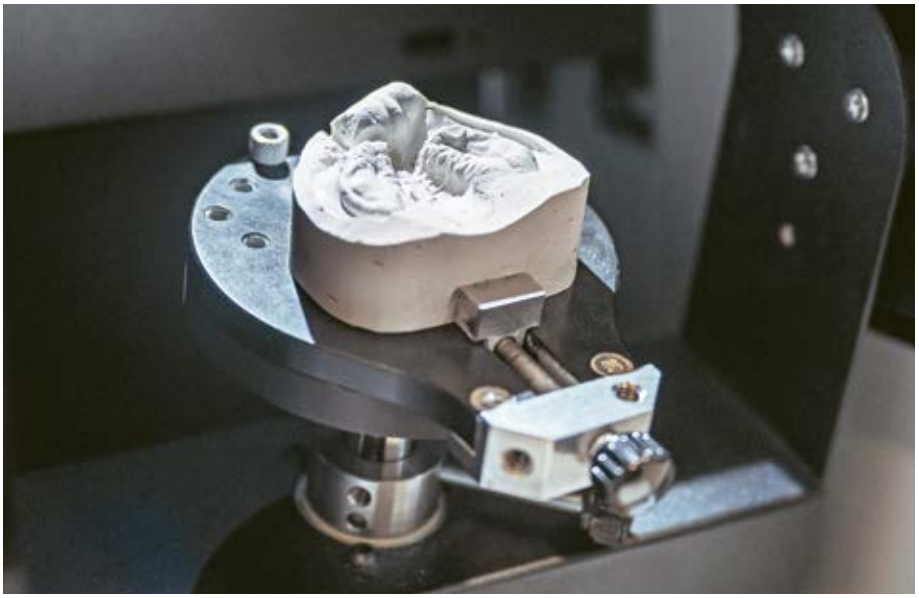
Burden-Reduced Cleft Lip and Palate Care and Healing

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 image of the cleft. This will enable 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; and 3) the closure of the malformation in a single surgical intervention instead of multiple interventions.

Update: Using intra-oral scans and video data from patients with orofacial clefts, the team built 3D models that can recognize specific malformations based on smartphone videos. Thus, the consortium was able to establish a new method of fast, low-cost and risk-free 3D data acquisition when compared to palatal plaster casts. Team members also used intra-oral scans and 3D printing methods to enable automated palatal plate design. Thus, the consortium has now succeeded in developing 3D-printed automatically designed palatal plates that are comparable to conventionally hand-designed and manufactured plates.

Collaborators: Srinivas Gosla Reddy (GSR Institute of Craniofacial Surgery, India); Andrzej Brudnicki (Institute of Mother and Child and Formmed Clinic, Poland); Markus Gross (Disney Research|Studios, Zurich); Syed Altaf Hussain (Sri Ramachandra Institute of Higher Education and Research (SRIHER), India); R.V.M. Surya Rao (Saveetha Medical College and Hospital, India).

Image: A plaster mould of a dental impression of a child's cleft palate sits in a machine that 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.



Lead Researchers

Andreas Mueller
University Hospital Basel &
University of Basel

Barbara Solenthaler
ETH Zurich

Living Microbial Diagnostics to Enable Individualized Child Health Interventions

Overview: Every year, millions of children 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 these changes can inform us about the body's current health status. This 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: During the past year, the consortium investigated how the engineered bacteria behave and function when introduced into the gut of various animal models. Specifically, its members studied how differential microbiota colonization, gut alterations and dietary factors affect the bacteria's ability to sense and record their surrounding environment. Longitudinal metabolomics studies have been completed in order to map a landscape of the environment that the bacteria encounter as they transit through the gut. In addition, the consortium is continuing to study longitudinal samples from mothers and babies living in Zimbabwe and Switzerland in order to gain insights into risk factors for malnutrition and stunting related to gastrointestinal dysfunction in children.

Collaborators: Andrew Macpherson (University of Bern); Kerina Duri (University of Zimbabwe, Zimbabwe); Tyrell Conway (University of Oklahoma, USA).

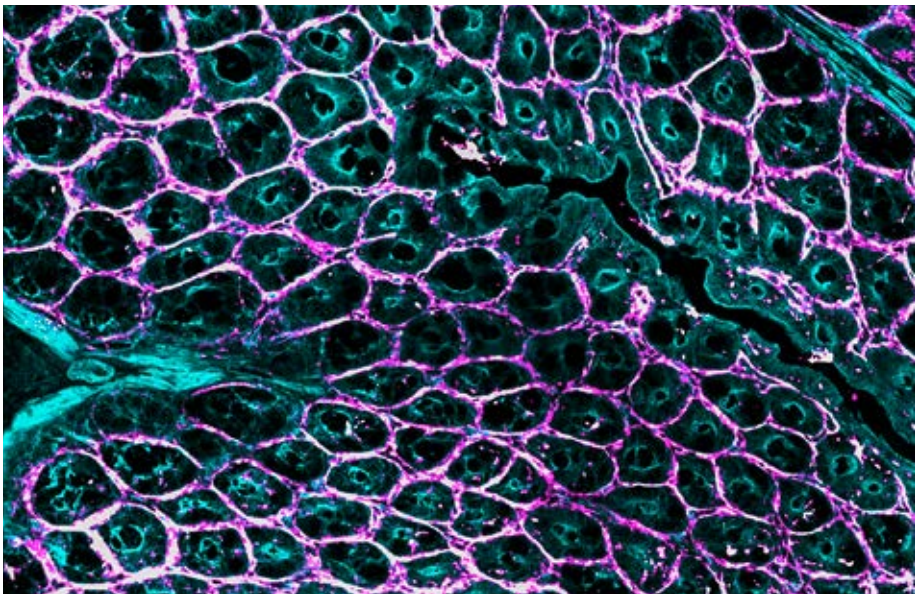
Image: A researcher in the Platt lab uses bacteria to engineer proteins with enhanced functionality. These methods are used to bioengineer bacteria to improve the efficiency of a novel technique called Record-seq.

Lead Researchers

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, its research will generate fundamental insights into microbiota, as well as preclinical insights into therapy efficacy and safety.

Update: The consortium has focused on establishing gnotobiotic models of human diseases and on probing the underlying mechanisms of disease. Its members have been developing technology for detailed animal phenotyping and testing vaccine or microbiological interventions to permit *in situ* microbiota engineering. The consortium has started to collect longitudinal samples from two clinical studies: 1) the study of microbiome maturation in very low birthweight infants and 2) the study of microbiota stability in inborn errors of metabolism conditions. A sample-analysis pipeline to track the identity of potentially pathogenic facultative aerobes over time has been established and the sequencing of the first patients is currently underway.

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

Image: Microscopic view of a cross-section of caecal tissue. The tissue is stained for actin (blue) and the extracellular matrix protein fibronectin (magenta/white). The circular structures visible in this section represent the single crypt structures of the gastrointestinal tract. In the actin staining, the epithelial brush border is visible (middle right), as well as some muscular and blood vessel structures (left). Credit: Ronja Rappold.

Lead Researchers

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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 serves as a rapid emergency response to the unprecedented challenge of the COVID-19 pandemic to the health and well-being of communities worldwide.

The overall objective is not only to quickly enable research that will help to mitigate medical and public health challenges in the short term, but also to contribute tangible solutions that will lead to better preparedness and reduced global disease burden over time. Fourteen research consortia are conducting projects as part of the FTC COVID-19 initiative, with support for up to 2.5 years.

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

Overview: 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 are combining artificial intelligence, portable chest X-ray machines and antigen-based diagnostic tests in order to enable and improve the diagnosis of COVID-19 patients in settings with limited resources.

Update: The researchers evaluated the diagnostic performance of an artificial intelligence software tool (CAD4COVID) combined with blood analysis in order to enable the automated evaluation of chest radiographs in suspected COVID-19 cases and improve the diagnosis of COVID-19 pneumonia. The team established triage and diagnostic centres in Lesotho and also evaluated the performance of a panel of novel antigen-based rapid diagnostics in these settings. To date, the team has provided SARS-CoV-2 testing to more than 2,400 adults and children seeking services at their testing sites.

Collaborators: Josephine Muhairwe, Irene Ayakaka (SolidarMed); Bram van Ginneken (Radboud University Medical Center, Netherlands); Morten Ruhwald (Foundation for Innovative New Diagnostics (FIND)).

Image: Within the MistraL mobile lab truck, a person with COVID-19-like symptoms receives a chest X-ray. The X-ray is then assessed using CAD4COVID and CAD4TB software to estimate the probability of the presence of COVID-19 pneumonia or tuberculosis. Credit: SolidarMed and Swiss TPH.

Lead Researchers

Klaus Reither
Swiss TPH

Niklaus Labhardt
Swiss TPH

peakPCR: Making DNA Analyses Faster and More Accessible

Overview: 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. With the aim of making DNA analysis faster and more accessible in point-of-care and resource-limited settings, the team is developing an innovative PCR instrument called *peakPCR* that will enable low-cost, real-time diagnostics for SARS-CoV-2 and other infections in under 30 minutes. 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.

Update: The team finalized the device design and established an automated process that will facilitate production scale-up of SARS-CoV-2 test cartridges. The device and test cartridges were evaluated and adapted for use in resource-limited settings. In addition, the team has started to develop novel sample preparation methods in order to further facilitate rapid testing in such settings. They are now exploring the application of the *peakPCR* device for other pertinent infectious diseases. This year, they participated in a large-scale schistosomiasis testing campaign in Zanzibar, in which *peakPCR* was used to screen more than 5,000 children in mobile laboratories at schools across the island.

Collaborators: Michele Gregorini, Philippe Bechtold (ETH Zurich).

Image: BRCCH researchers are developing an affordable and accurate "rapid PCR test" with the goal of making advanced diagnostics available in point-of-care and resource-limited settings. Credit: Diaxxo AG.

Lead Researchers

Wendelin Stark
ETH Zurich

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

Overview: Some of the central challenges in mitigating the COVID-19 pandemic are the difficulty of detecting infection and the emergence of mutated variant strains. This consortium brings together molecular engineers, computational biologists and clinical scientists with the aim of overcoming current limitations in genomic surveillance and the prediction of future variants of SARS-CoV-2. First, the consortium aims to develop a scalable platform for SARS-CoV-2 detection and genomic surveillance using innovative molecular barcoding and deep-sequencing techniques. Second, it aims to identify and predict future variants of SARS-CoV-2 using AI and deep learning. This approach also has significant future application potential for different types of coronaviruses and other viral threats.

Update: The team has successfully established a molecular barcoding method for tagging individual patient RNA samples, which is then used for the multiplexed detection of selected viral genomic regions by deep sequencing. This method has been benchmarked for high sensitivity and specificity, comparable to the established standard of qRT-PCR, and it has been applied to large-scale human patient RNA samples. The team has also established deep mutational learning (DML) in order to interrogate combinatorial mutations in the receptor-binding domain of SARS-CoV-2 for their impact on cellular infection and antibody escape. This shows that DML enables the predictive profiling of variants and may be used to guide decision-making for therapeutic antibody treatments for COVID-19.

Image: Researchers work on high-throughput diagnostic methods for SARS-CoV-2.

Lead Researchers

Sai Reddy
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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

Lead Researchers

Janos Vörös
ETH Zurich

Michael Osthoff
University Hospital Basel

Overview: This project aims to develop a mobile and rapid diagnostic test system for COVID-19. The incubation period for SARS-CoV-2 lasts several days, during which time patients do not experience any symptoms. This leads to the creation of a blind spot: many people who are transmitting the disease are currently undiagnosed. Also, state-of-the-art rapid tests cannot reliably diagnose patients in the early stages of infection due to their limited accuracy. The only way to remedy this blind spot is to develop a new type of diagnostic test that is mobile, fast, cheap, lab-independent and accurate. This diagnostic test based on lateral flow assays will optimize the sensitivity and precision of COVID-19 testing.

Update: The team has enhanced the design and performance of the readout device prototype and has also developed methods that will facilitate automated operation and use in clinical settings. To date, team members have successfully developed a COVID-19 lateral flow assay that is highly sensitive and compatible with different sample types. The team is now embarking on a validation study to assess the performance of the diagnostic test in a clinical setting in comparison with commercially available COVID-19 diagnostics.

Collaborators: Noé Brasier (University Hospital Basel); Samuele Tosatti (SuSoS AG); Oliver Weingart (konplan AG); Alexander Tanno (ETH Zurich/Hemetron).

Image: The consortium is working to create a rapid point-of-need diagnostic test. A sample droplet is loaded onto the sample pad (lower left corner) of the assay. The viral proteins in the sample are immobilized and labelled. The readout device then accurately quantifies the labelled proteins and displays the result on the screen. Credit: Alexander Tanno, Hemetron AG.

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

Overview: The DAVINCI consortium is developing a novel COVID-19 diagnostic test based on saliva, which is designed for maximum simplicity in handling in order to enable self-testing at home. The DAVINCI test can detect antigens of and antibodies against SARS-CoV-2 virus at the same time. Hence, it can detect either an acute infection with SARS-CoV-2, past exposure to the SARS-CoV-2 virus or a successful vaccination with antibody production. This unique test will enable each user to evaluate his/her own individual immune status within 15 minutes, answering questions regarding individual protection and response to COVID-19 vaccinations. Ultimately, this rapid diagnostic approach aims to contribute to improving healthcare during the current pandemic and beyond.

Update: The consortium has completed a functional prototype for a home-use saliva-based COVID-19 test without the need for sample manipulation or the addition of reagents. It has also performed a small study to assess ease of use by untrained users. Furthermore, a mobile phone application has been developed to guide usage, perform result analysis and enable connectivity to relevant databases and services. Finally, over 1,000 saliva samples have been collected to date in order to carry out further validation of the device.

Collaborators: Frank Dieterle (SwissTPH); Samantha Paoletti (CSEM); Peter Spies (FHNW); Vanja Ivancevic, Pascal Winnen (HEMEX); Saso Jerzernik (BioInitials); Nila-Pia Rähle (Effectum Medical); Miodrag Savic (University Hospital Basel).

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

Lead Researchers

Daniel Paris
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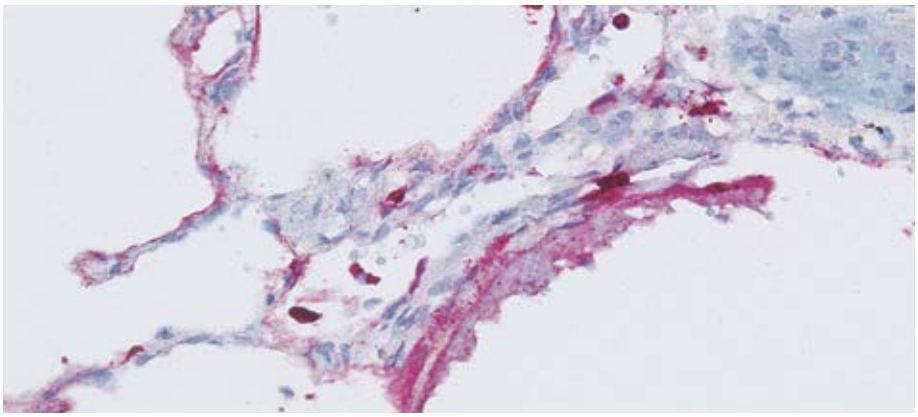

Lessons from the Deceased to the Living and Back: Investigation of SARS-CoV-2 Interactions with Human Cells, Tissues and Organs in a Unique Basel-Region Cohort of Autoptically Examined COVID-19 Patients

Overview: Previously, very little was 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 performs *in situ* investigations of how SARS-CoV-2 interacts with tissues and organs derived from deceased patients and patients suffering from severe COVID-19. The project is continuously contributing insights into the pathogenesis of COVID-19, and its holistic approach is paving the way for more efficient medical interventions for this disease.

Update: The project has uncovered the central roles of disordered microcirculation, thrombosis and irregular new vessel formation in the lungs, hearts and lymph nodes of COVID-19 patients. Its researchers have determined that SARS-CoV-2 is neither cardio-, lympho- or neurotropic; instead, these organs are fields of significant collateral damage. The consortium's investigations have indicated SARS-CoV-2 pancreato-/insulotropism and tropism to the abdominal fat. This mechanistically explains interrelations between COVID-19 and human metabolism. They have shown that COVID-19 is a multi-phase disease involving initial viral replication and spread, followed by an interferon-mediated immune response, coagulopathy and ending with immunopathology. Finally, changes in the expression level of the cell fitness marker *hFwe-Lose,* which can easily be read out on nasopharyngeal swabs, were identified as relevant regarding the prognostication of COVID-19 outcomes in vaccine-naïve individuals.

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

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 o'clock), as well as in isolated desquamated macrophages (intensively staining single cells). Credit: Alexandar Tzankov, Institute of Pathology, University Hospital Basel.

Lead Researchers

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

Overview: This project is investigating B cell immunity in convalescent COVID-19 patients with the aim of identifying high-affinity antibodies against SARS-CoV-2 that could be further harnessed for therapeutic interventions. It combines innovative approaches in high-throughput testing of SARS-CoV-2 peptides, B cell receptor analysis at the single cell level and related antigen-affinity assays to interrogate the antibody repertoire of these patients. Overall, the project results will be invaluable for understanding B cell immunity in healthy, immunocompromised and vaccinated individuals and for identifying novel immunotherapeutic agents against SARS-CoV-2 in the future.

Update: Thus far, the consortium has optimized the experimental pipeline and adapted it for large-scale testing of clinical COVID-19 samples. The team has started to generate single cell B cell receptor (BCR) repertoires directly from convalescent COVID-19 patients. Additionally, team members are analysing the BCR repertoires of patients infected with either wild-type or variants of SARS-CoV-2. Recently, the consortium has also contributed new insights into the development of long-lived T cell memory following acute SARS-CoV-2 infection.

Collaborators: Randall Platt (ETH Zurich).

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

Lead Researchers

Andreas Moor
ETH Zurich

Yakir Guri
University Hospital Basel

ISINC-19: Immune Senescence in COVID-19

Overview: 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 disease course and outcomes. The team is exploring 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.

Update: The team has examined the metabolomic and inflammatory signatures of plasma from COVID-19 patients with various clinical manifestations. They have identified that COVID-19 patients harbour distinctive, abnormal metabolomic signatures that are associated with immune dysregulation and systemic inflammation. By mapping inflammation trajectories based on plasma analysis, the team determined that patients could be grouped into three categories of disease severity. The team is now investigating the immuno-metabolic mechanisms underlying varying COVID-19 severity. In parallel, they have begun to use repurposed drugs that impact mitochondrial function in order to evaluate their effects on pathogenic immune responses.

Collaborators: Daiana Stolz (University Hospital Basel).

Image: Symptomatic and asymptomatic blood cell samples are collected and preserved in liquid nitrogen in the course of the ISINC-19 study. Credit: Sarah Roffeis.

Lead Researchers

Christoph Hess
University of Basel & University of Cambridge

Glenn Bantug
University of Basel

Christoph Berger
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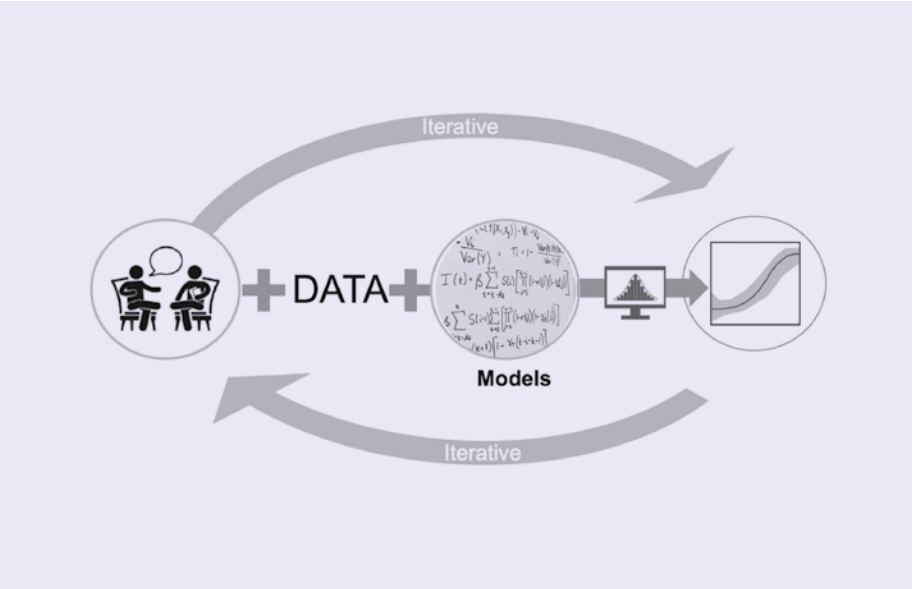

Using Model-Based Evidence to Optimize Medical Intervention Profiles and Disease Management Strategies for COVID-19 Control

Overview: Evidence-based guidance is critical in designing optimal intervention profiles and deployment strategies for medical interventions such as vaccines. This project seeks to harness mathematical modelling and machine learning approaches to guide and optimize clinical and public health strategies for diagnostics, therapeutic interventions, disease surveillance and management in the emergency response to the COVID-19 pandemic. Overall, this consortium's evidence-based models are contributing scientific insights in order to support public health policies for COVID-19 in Switzerland.

Update: The consortium has developed an open-source individual-based model of SARS-CoV-2 transmission dynamics named OpenCOVID. As part of the Swiss National COVID-19 Science Task Force and the Federal Office of Public Health, team members provided model-based evidence to guide policy decision-making regarding non-pharmaceutical interventions under varying vaccination strategies in Switzerland. Secondly, they applied their models in order to address the potential impact of new variants of concern on public health burden. Thirdly, they developed new analyses of serological data in order to estimate cumulative incidence and antibody decay. Finally, they have begun to investigate the future effects of long-term vaccination strategies, immunization rates and novel COVID-19 medical interventions.

Collaborators: Andrew Shattock, Sherrie Kelly, Epke Le Rutte (Swiss TPH); Sarah Kadelka, Judith Bouman (ETHZ).

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

Lead Researchers

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Swiss TPH

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ETH Zurich

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

Overview: Acute respiratory distress syndrome (ARDS) is a frequent cause of critical illness and mortality in COVID-19 patients. Supportive therapeutic strategies for ARDS often include the use of mechanical ventilation. However, patients may be subject to ventilator-induced lung injury, which can lead to severe lung damage and increased mortality. The aim of this project is to develop practical solutions that reduce the risks associated with the use of mechanical ventilation, especially those associated with low-cost/do-it-yourself ventilators and off-label use that are now available in many resource-limited settings.

Update: The consortium members assessed the performance of multiple low-cost ventilators in an experimental setting using an artificial lung model. Following this, they successfully integrated a novel pressure sensor into the low-cost ventilator chosen for further study and tested the system for performance and triggering behaviour. They also developed an add-on system in order to integrate a microscopic pressure sensor into the tip of an endotracheal tube. Finally, the team set up a functional *in vitro* test bench consisting of a mechanical lung simulator, pressure sensors and hardware and software components. They are now investigating the effects of *in vivo* conditions on the performance of the LCV system and supporting algorithms.

Collaborators: Sören Fricke (CSEM).

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

Lead Researchers

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

Overview: This project harnesses CRISPR-based technologies in order to identify factors that are crucial for SARS-CoV-2 to infect and cause disease in humans. The team is using a combination of *in vitro*- and *in vivo*-based strategies in order to identify and validate novel therapeutic targets for combatting SARS-CoV-2. In this way, the project aims to reveal novel therapeutic strategies for future COVID-19 patients.

Update: In order to identify biological factors that are important for SARS-CoV-2 infection, the team is performing CRISPR screening using different human cell types infected with SARS-CoV-2. To date, the consortium has established methodologies for producing SARS-CoV-2 and variant pseudoviruses for experimental purposes. They are currently developing assays in order to study the entry of these pseudoviruses into different types of infected human cells. These studies aim to reveal the mechanisms by which the virus infects human cells and causes disease in order to aid future therapeutic development.

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

Lead Researchers

Randall Platt
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BRCCH-EDCTP COVID-19 Collaboration Initiative

In 2021, the BRCCH and the European & Developing Countries Clinical Trials Partnership (EDCTP) established a new partnership to drive united and interdisciplinary efforts in advancing impactful health interventions for COVID-19, particularly in LMIC settings. The initiative supports three collaborative projects co-led by BRCCH- and EDCTP-funded researchers across COVID-19 immunology, diagnostics and health screening strategies. Research activities started in January 2021 and will continue for two years.

Improving Access to SARS-CoV-2 Screening and Testing through Community-Based COVID-19 Case-Finding and the Use of Digital Solutions in Lesotho and Zambia

Overview: In many resource-limited settings, weak healthcare systems are already struggling to cope with the SARS-CoV-2 pandemic. Research teams in Lesotho and Zambia are investigating the effects of community-led interventions, rapid point-of-care diagnostics and swab self-collection in mitigating the COVID-19 epidemic in these countries. Innovative and locally adapted mitigation strategies for improving the COVID-19 care cascade, protecting communities and healthcare workers and in return increasing access to essential services are desperately needed. This consortium convenes expertise from various disciplines and institutions to improve the COVID-19 care cascade, reduce community transmission and mitigate the impact on service utilization in resource-limited settings. Through close collaboration with the local communities and health authorities and the utilization of locally developed solutions, the project will provide a sustainable and locally grounded COVID-19 response, with an impact even beyond the project period.

Collaborators: Lucia Fernandez Gonzalez, Niklaus Labhardt, Alain Amstutz (Swiss TPH); Musonda Simwinga (Zambart, Zambia); Josephine Muhairwe, Bulemba Katende (SolidarMed); Helen Ayles (Zambart, Zambia & London School of Hygiene and Tropical Medicine, UK); Maria Ruperez Larrea, Sian Floyd (London School of Hygiene and Tropical Medicine, UK); Eveline Klinkenberg (Independent consultant); Petra de Haas (KNCV Tuberculosis Foundation); Samuel Schumacher (Foundation for Innovative New Diagnostics (FIND)).

Image: Researchers undertake community outreach in remote areas in Lesotho in order to increase access to essential health services. Credit: SolidarMed and Swiss TPH.

Lead Researchers

Klaus Reither
Swiss TPH

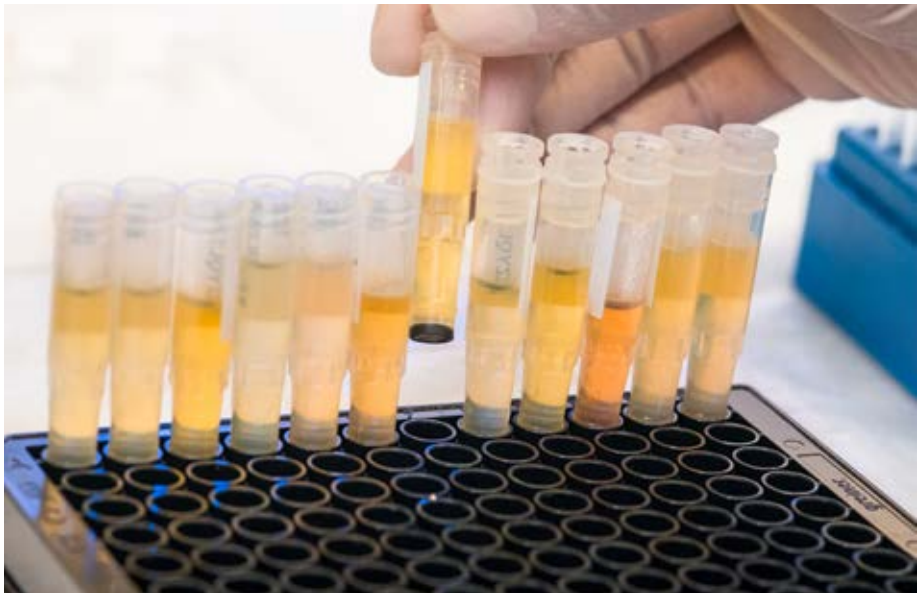
Dr Kwame Shanaube
Zambart, Zambia

COVID-19 Antibody Repertoires in Infection and Vaccination

Overview: This consortium aims to investigate B cell-mediated immunity to SARS-CoV-2 infection in different health states, with the purpose of gaining new insights into how vaccines can be improved to generate optimized neutralizing antibody responses. Specifically, the researchers are investigating and comparing the effects of SARS-CoV-2 infection on the antibody repertoire in patients who contract the virus through natural means, COVID-19 patients who also suffer from HIV, and vaccinated individuals. This project provides unique access to diverse participant samples and combines complementary laboratory techniques in order to address key questions related to our understanding of the immune response in COVID-19. Its research may identify better antibodies for evaluation and progress into treatment and prevention trials for SARS-CoV-2. The groundwork for this project will also pave the way for the next waves of the pandemic and for the rapid investigation of other emerging viruses.

Collaborators: Katie Doores (King's College London, UK); Yakir Guri (University Hospital Basel).

Image: A scientist preparing patient samples for SARS-CoV-2 antibody testing. Credit: James Gathany.



Lead Researchers

Andreas Moor
ETH Zurich

Julie Fox
King's College London, UK

African-European Partnership for the Development and Deployment of Rapid SARS-CoV-2 RNA and Antigen Detection Assays

Overview: Despite recent developments in SARS-CoV-2 vaccines, the long timeline for worldwide vaccine coverage and the threat of new emerging viral mutants mean that the most effective control measure remains the detection of infected cases. This project aims to advance novel and rapid COVID-19 diagnostic technologies tailored for resource-poor and emergency settings. Including partners in nine countries, the consortium will combine efforts to evaluate and deploy a rapid lateral flow diagnostic assay and a portable PCR device, both to be hosted in a mobile suitcase lab for implementation at point of need in LMICs. The mobile suitcase lab has the potential to increase access to diagnostics in remote settings. The case will be powered by a solar panel and the reagents can be kept at an ambient temperature, decoupling it from dependence on refrigeration. The consortium is planning a multi-country blind diagnostic test evaluation study to assess diagnostics *in situ* across various environmental conditions.

Collaborators: Alexander Tanno, Michele Gregorini (ETH Zurich); Anavaj Sakuntabhai (Institut Pasteur, France); Michael Frimpong (Kwame Nkrumah University of Science and Technology, Ghana); Dia Ndongo (Institut Pasteur de Dakar, Senegal); Philippe Dussart (Institut Pasteur de Madagascar); Olusegun George Ademowo (University of Ibadam, Nigeria); Sheila Makiala (Institut National de Recherche Biomédicale du Zaire (INRB)); Kamal Eltom (University of Khartoum, Sudan); Julius Boniface Okuni (Makerere University, Uganda).

Image: An open case shows the lab components for a rapid PCR assay *(peakPCR)*. The portable case enables researchers to perform the assays at point of need. Credit: Finja Rausch.

Lead Researchers

Janos Vörös
ETH Zurich

Wendelin Stark
ETH Zurich

Ahmed Abd El Wahed
Leipzig University, Germany

Postdoctoral Excellence Programme

The Postdoctoral Excellence Programme (PEP) aims to foster the next generation of scientific leaders who will pursue interdisciplinary research in order to address critical unmet needs and challenges in global paediatric health. The projects range in topic from digital tools for improving paediatric medicine to sepsis detection. Together with established host Principal Investigators and Collaborators, five highly talented PEP Fellows will implement translational and ambitious research projects over the next three years.

Harnessing Machine Learning and Mechanistic Modelling for Personalized Radiotherapy of Paediatric Diffuse Midline Glioma

Overview: Diffuse midline glioma is a fatal disease primarily affecting children between four and seven years of age, which currently has no curative treatment. Owing to the delicate location of these tumours in the brain, treatment options and surgical interventions are greatly limited. Radiotherapy (RT) is one of the few life-prolonging treatments, but its therapeutic efficacy varies between individuals. Also, the current one-size-fits-all therapy is mostly based on clinical experience in adults. The researchers will use a combinatorial approach by employing two powerful tools originating from different research fields: machine learning and the modelling of tumour growth with differential equations. This combination of models facilitates not only the identification of which children will benefit from conventional RT, but also if and how the impact of RT can be maximized by changing its scheduling and dosing. The goal is to develop a digital health tool that is readily translatable to clinics worldwide in order to guide doctors in designing optimal treatment strategies for affected children and their families.

Image: The combination of machine learning and the modelling of tumour growth with differential equations will enable the creation of a digital health tool that will improve the quality of life of children diagnosed with diffuse midline glioma.

Lead Researchers

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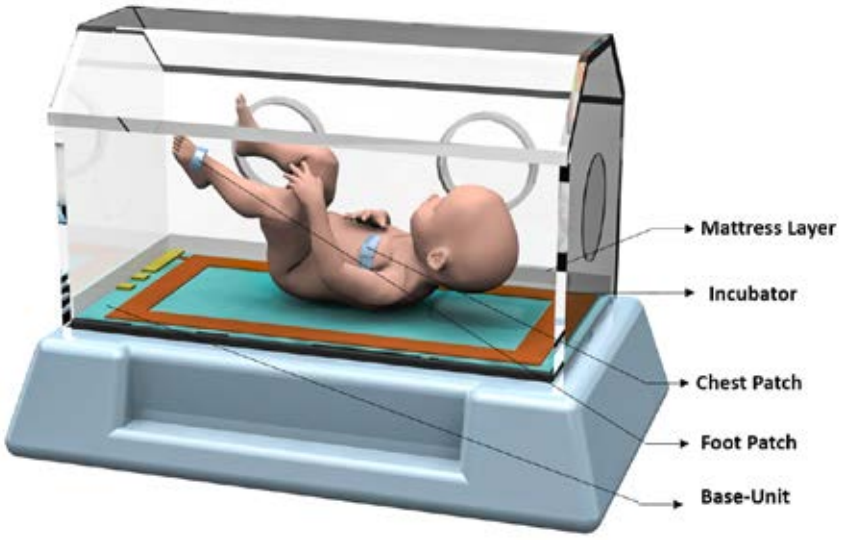


Patch-IT: Multi-Sensor Sensor Nodes for Continuous Vital Sign Monitoring to Identify Novel Digital Biomarkers for Sepsis Detection in Neonatal Intensive Care

Overview: Sepsis is a life-threatening bodily response to infection. Moreover, neonatal sepsis has a high incidence globally and is a major cause of mortality worldwide. In the absence of specific treatment, efficient patient monitoring and management are crucial for better patient outcomes. However, current monitoring platforms attach multiple wires to the neonate's fragile and underdeveloped skin, thus creating a web of wires and on-body electrodes that use aggressive adhesives. In addition to the risk of injury and skin lacerations, this impedes skin-to-skin contact between parent and child. The team aims to develop a multi-sensor electronic epidermal system, PATCH-IT, that incorporates wire-free, battery-free, non-invasive and autonomous monitoring of multiple vital signs continuously and in real time. PATCH-IT thus provides multi-sensor data specific to the needs of sepsis monitoring and in-sensor data analytics empowered by state-of-the-art sensor fusion algorithms personalized to every patient. The overarching goal is to provide a wireless sytsem for the continuous monitoring of vital signs in neonates and a more effective detection of sepsis via digital biomarkers for better disease management and patient outcomes.

Image: PATCH-IT integrated into an incubator in NICU. The base unit is placed below the mattress and the c-patch is placed on the neonate's chest, while the f-patch is placed on the neonate's foot. Credit: Kanika Dheman.

Lead Researchers

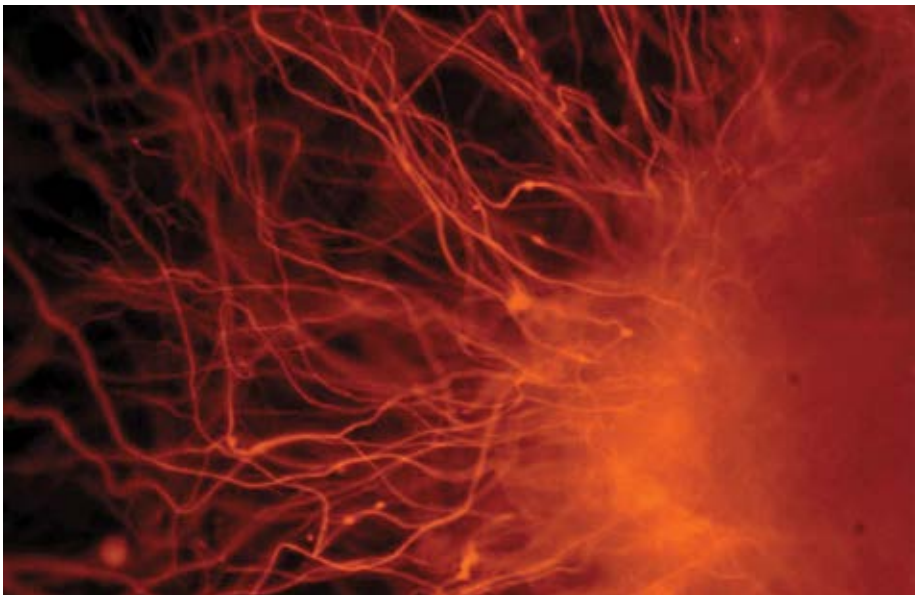
Kanika Dheman
ETH Zurich

Michele Magno
ETH Zurich

Developing Novel Drug Strategies for the Treatment of Fragile X by Functional Screening of Human Pluripotent Stem Cell Models

Overview: Fragile X Syndrome (FXS) is the most common form of genetically inherited intellectual disability. Unfortunately, most FXS treatments address the symptoms and not the cause of the disease and hence are neither very effective nor curative. In addition, the existing drugs used for treatment must be taken throughout the patient's life and may pose a financial burden on them and their families, especially low-income families and the healthcare systems of low-income countries. FXS occurs due to the epigenetic silencing, or non-expression, of a specific gene, FMR1. The overarching goal of this project is to identify and test new drugs using human stem cells with the ability to induce the re-expression of FMR1 and reverse FXS symptoms and effects. The project has three aims: 1) to establish baseline levels of FMR1 expression and downstream targets in normal and FXS stem cells; 2) to screen novel categories of drug compounds; and 3) to establish organoids, a type of tissue culture, from FXS stem cells in order to perform anatomical validation of drug efficacy. Taken together, the team aspires to develop novel prenatal or early postnatal strategies for treating FXS.

Image: An *in vitro* stem cell was directed to become a neuron showing the characteristic axons branching out from the soma of the cell. These neurons, which are derived from human embryonic stem cells, can be used to study how the human brain develops and to model neurological disorders. Credit: Nissim Benvenisty Lab, Azrieli Center for Stem Cells and Genetic Research, Hebrew University of Jerusalem.



Lead Researchers

Keith Gunapala
University of Basel

Verdon Taylor
University of Basel

Nissim Benvenisty
The Hebrew University of Jerusalem, Israel

Electronic Clinical Decision Algorithms and Machine Learning to Improve Quality of Care and Clinical Outcomes for Sick Young Infants in Resource-Limited Countries

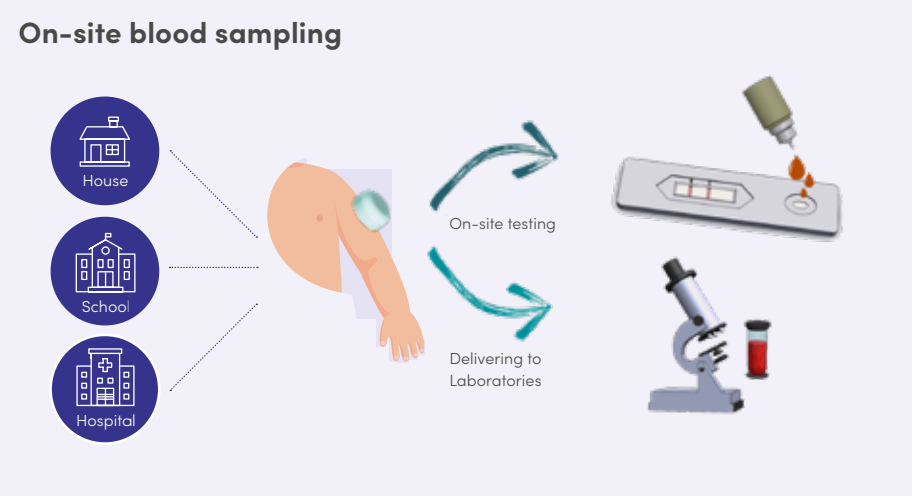
Overview: The appropriate clinical management of sick young infants requires care from highly trained and specialized healthcare workers, who are rarely available in primary care health facilities in LMICs. Electronic Clinical Decision Support Algorithms (eCDSAs) may offer a solution by providing guidance to health workers for evaluating and managing young patients. However, no such tool has been validated or tested for managing sick young infants in outpatient care settings in LMICs. The team will evaluate the effects of an eCDSA for neonates and young infants on the quality of care and clinical outcomes among young infants in five LMICs. The researchers are aiming to enhance the prognostic and diagnostic performance of the algorithm using machine learning methods. The outputs of the project have the potential to impact millions of sick young infants in LMICs and to ultimately reduce mortality in this high-risk population.

Image: Health workers in Senegal pilot test the electronic clinical decision support tool to manage sick young infants. Credit: Gillian Levine.

Lead Researchers

Gillian Levine
Swiss TPH

Tracy Glass
Swiss TPH



Bioinspired, Low-Cost Device for Minimally Invasive Blood Sampling

Overview: The majority of medical decisions depend on laboratory results, and blood sampling is the most prevalent route for disease diagnosis and monitoring. This project proposes to develop a versatile microsampling device for the collection of blood with minimal invasiveness, low manufacturing costs and sufficient volume retrieval for point-of-care tests or laboratory analysis. This device may be particularly suited for children, where traditional blood draws using needles can cause distress. A prototype will be manufactured via 3D printing and validated pre-clinically and in combination with a commercially available point-of-care test for the detection of malaria. Being minimally invasive and also versatile when combined with POC methods, this device could turn out to be a game-changing approach that would benefit both the paediatric population and LMICs.

Image: Researchers are developing a bio-inspired and patient-friendly device for blood sampling that is minimally invasive and low cost, which may allow for point-of-care tests or laboratory analysis. Credit: Nicole Zoratto.

Lead Researchers

Nicole Zoratto
ETH Zurich

Jean-Christophe Leroux
ETH Zurich

BRCCH researchers are working together with international collaborators in order to enable and improve the diagnosis of COVID-19 patients in settings with limited resources. The MistraL team in Lesotho has provided SARS-CoV-2 testing to more than 2,400 adults and children seeking services at its testing sites to date. Credit: SolidarMed and Swiss TPH.

Outputs and Media Presence

The researchers and clinicians involved in BRCCH-funded research projects have been extremely productive. The BRCCH commends its partners for their research achievements and dissemination efforts.

36 published papers in peer-reviewed journals

80 research presentations (talks, seminars and posters) either online or in person by researchers discussing BRCCH-funded work

3 patent applications submitted by FTC COVID-19 consortia

8 capacity-building events (educational lectures, conference organization, outreach activities, training sessions)

21 research disseminations in the news and media via interviews and reports

Burden-Reduced Cleft Lip and Palate Care and Healing

India's Ambassador to Switzerland, H.E. Ms Monika Kapil Mohta, welcomed Dr Andreas Mueller and his team along with Dr Charlotte Werthemann (Head of External Affairs, University Hospital Basel) to her residence, where they engaged in discussions about the ongoing partnership between the MIP consortium and the Indian healthcare system. The ambassador lauded the efforts of University Hospital Basel and the University of Basel in encouraging collaborative research activities with the goal of delivering a holistic approach to healthcare for all. Credit: Embassy of India, Bern, Switzerland.

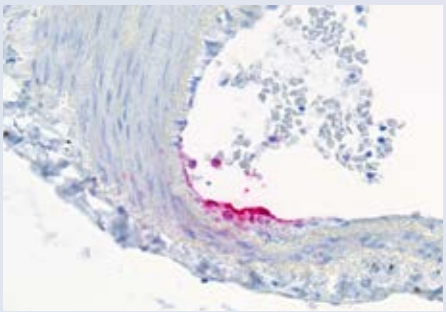
Precision Microbiota Engineering for Child Health

In July 2021, Prof Emma Slack and colleagues published a research article entitled "A rationally designed oral vaccine induces immunoglobulin A in the murine gut that directs the evolution of attenuated *Salmonella* variants" in the renowned journal *Nature Microbiology.* The consortium's work represents a major step in developing mucosal vaccines that can alter the gut microbiome. Credit: Dr Alyson Hockenberry, U-SYS ETHZ/EAWAG.

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

The DAVINCI consortium, led by Prof Daniel Paris, gave the first public presentation of their earliest prototype at the Swiss Symposium in Point-of-Care Diagnostics in October. Their disposable rapid COVID-19 diagnostic enables self-testing for both antigens and antibodies based on saliva. Credit: DAVINCI consortium.

Lessons from the Deceased to the Living and Back



This year, this consortium, led by Prof Alexandar Tzankov, has made important contributions to advancing the fields of COVID-19 pathology and immunology. The team has published 23 peer-reviewed articles to date and has made several landmark discoveries in COVID-19 clinical pathogenesis and markers of disease prognosis. Credit: Prof Alexandar Tzankov, Department of Histopathology and Autopsy, University Hospital Basel.

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

Prof Melissa Penny, Prof Roland Regoes and Dr Andrew Shattock were active members of the Swiss National COVID-19 Science Task Force. The consortium provided its expertise in the computational modelling of COVID-19 to support national decision-making during the course of the pandemic in collaboration with the Federal Office of Public Health (Bundesamt für Gesundheit BAG). Credit: Joachim Pelikan, Swiss TPH.

peakPCR: Making DNA Analyses Faster and More Accessible

Based on their novel *peakPCR* technology for COVID-19 diagnostics, the consortium, led by Prof Wendelin Stark, established a new start-up company named Diaxxo AG. The device offers low-cost portable PCR testing in under 30 minutes. The consortium is now expanding the device's use to other infectious diseases, including those that are highly prevalent in LMICs such as schistosomiasis. Credit: Diaxxo AG.

Meet the Advisory Board

The BRCCH's activities benefit from the involvement of the members of the BRCCH Strategic Scientific Advisory Board (SSAB). The Centre is pleased to introduce the Board's members here, some of whom have been advising the BRCCH since its operations began three years ago and some of whom joined the Centre this past year. Together, its 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 Director Emeritus of 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 Professor of Paediatrics at the Children's Hospital of Philadelphia (CHOP) and the University of Pennsylvania, USA. He also directs 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 a 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 the scaling up of 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 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.

Prof Margaret Gyapong joined our Strategic Scientific Advisory Board in 2021. She is the Director of the Institute of Health Research at the University of Health and Allied Sciences in Ho, Ghana, and holds professorial and adjunct professorial positions at the University of Health and Allied Sciences and Georgetown University in Washington DC, USA. Her research focuses on the socio-cultural aspects of tropical diseases, implementation research, maternal and child health and capacity building. She has a background in medical anthropology and cultural epidemiology and received the EDCTP Outstanding Female Scientist Award from the European & Developing Countries Clinical Trials Partnership (EDCTP) in October 2021.

BRCCH: Prof Gyapong, which aspects of your expertise are you planning to implement as a member of the BRCCH's Advisory Board?
Prof Margaret Gyapong: My background is in medical anthropology and epidemiology, and I engage a lot with health systems and implementation research. So basically, I want to ensure that research is not done for research's sake, but that it is relevant to the people who need the results of that research.
BRCCH: Which topics are you most interested in?
Prof Gyapong: I've worked on multiple topics over the years, but my main interest is in neglected tropical diseases. I also work in the areas of malaria, maternal and child health and demographic surveillance systems.
BRCCH: Please tell us about some of your current projects.
Prof Gyapong: One of my projects focuses on female genital schistosomiasis (FGS), a disease caused by a water parasite that affects both the urinary and genital tract of infected individuals. FGS affects 50 to 60 million adolescent girls and women worldwide, but has been largely neglected until recently. When an individual is affected by FGS, she is usually referred to a gynaecologist, who approaches the treatment from the perspective of a regular gynaecological problem without asking questions about the patient's background, such as where they live, what their water source is, etc. As a result, the opportunity to treat these women with available and appropriate medicines is missed. We're now trying to address this problem in a holistic way: training health workers to be able to diagnose and treat the disease effectively, creating awareness about FGS in schools and communities, engaging with water and sanitation departments to improve water sources being provided to local communities and working with neglected tropical diseases programmes as they implement mass administration of praziquantel for the treatment of schistosomiasis in schools and communities. Another project I am working on focuses on adolescent pregnancy, which is a major issue in some of the districts in the Volta region of Ghana. We are working with adolescent girls, the District Health Directorate, community leaders and other stakeholders to understand the causes and how we can address the issue. Our goals are to educate young women about how they can protect themselves from unwanted pregnancies and to support parents in engaging in open conversations with their daughters about sexuality.
BRCCH: From your perspective, what is most needed to improve paediatric health in low- and middle-income countries?
Prof Gyapong: I think commitment and a proper understanding of the problem are pre-eminent. We need to make sure that we have appropriate data about the problem, that we generate knowledge about the diseases we are interested in addressing and that we assess interventions in the paediatric population and what their impact is in real life. My experience has been that the results can be very diverse and depend on many factors. One size doesn't fit all.
BRCCH: You've had an impressive career as a scientist and promotor of research, you've raised three daughters and you still have many ideas and goals you want to accomplish. What motivates you?
Prof Gyapong: The fact that I can do work that will bring a change in people's lives. That motivates me to do more. I have done a lot of research that has influenced policy change and I've seen implemented policies working in real life. It warms my heart to be able to relate to those policies and programmes that are running in Ghana today. That is what keeps me going: knowing that when I do my work and engage properly with the right people, the results will be used to make a difference in the life of a mother and her child.

Interview conducted by Irène Dietschi.

"I want to ensure that research is not done for research's sake, but that it is relevant to the people who need the results of that research."

Margaret Gyapong

Governance and Finances

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's academic leaders, Director Prof Georg Holländer and Vice Director Prof Sai Reddy, are 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
and President of
the University of Basel

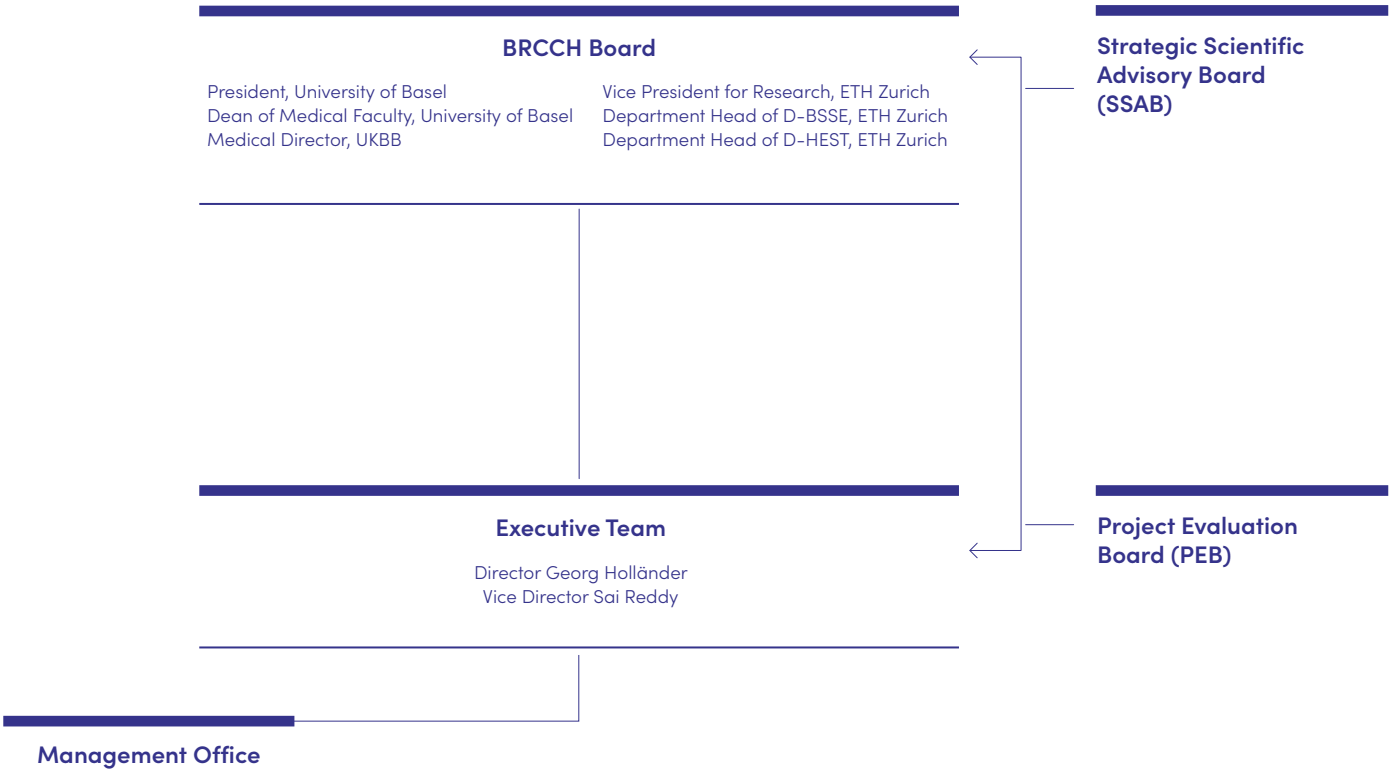
Prof Detlef Günther
Co-Chair of BRCCH Board and
Vice President for Research and
Corporate Relations at ETH Zurich

Prof Primo Schär
Dean of the Medical Faculty
at the University of Basel

Prof Daniel Müller
Head of the Department of
Biosystems Science and Engineering
(D-BSSE) at ETH Zurich

Prof Urs Frey
Medical Director
of University Children's Hospital Basel

Prof Stephen Ferguson
Head of the Department of
Health Sciences and Technology
(D-HEST) at ETH Zurich



Finance

The BRCCH benefits from a generous donation of a total of CHF 115 Mio from Fondation Botnar, which will support its activities from 2019 to 2028. This budget is equally shared between the University of Basel and ETH Zurich and has allowed the BRCCH to establish a research project portfolio currently comprising the Multi-Investigator Programme, the Fast Track Call for COVID-19 Research, the Postdoctoral Excellence Programme and the Principal Investigator Initiative. The Centre's next steps include the continuation of plans for assistant professorships to be initially supported by the BRCCH.

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