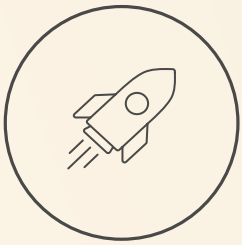
BRC CH Botnar Research Centre for Child Health

Annual Report 2022
Botnar Research Centre for Child Health

University of Basel ETH zürich

Supported by Fondation Botnar

Facts and Numbers 2022



Jan 1, 2019
Start of Operations

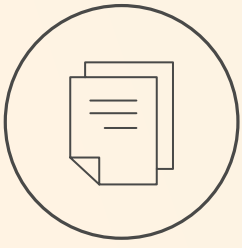
4
Partner Institutions

47
International Research Collaborations

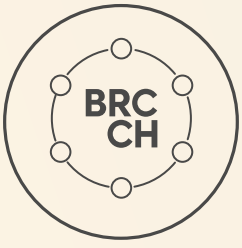
80
Lead Researchers

37.6
Mio CHF in Research Project Support

29
Research Projects



77
Scientific Outputs

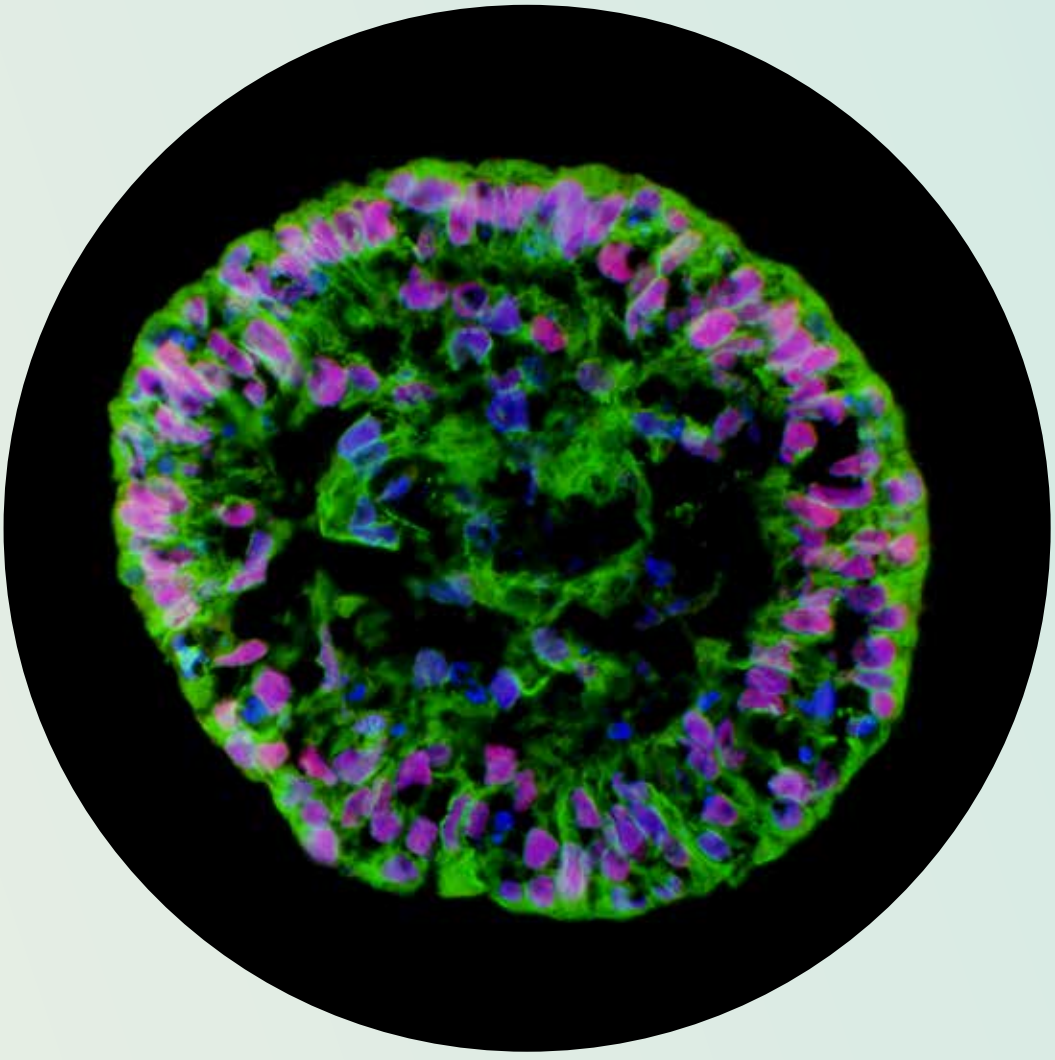


5
Research Programmes

The world has witnessed an improvement in paediatric health over the last decades. Still, more work needs to be done and global challenges continue to threaten young people. This vulnerable population, especially small children in low-resource settings, is particularly at risk of long-term health implications and mortality in part caused by infectious diseases such as malaria, pneumonia and gastrointestinal infections[1, 2]. The rise in non-communicable diseases in adolescents lays an additional burden on young people. The health and well-being of young people across all age groups is further impacted by diverse socio-economic and environmental factors, including inequities in healthcare access and quality as well as the global challenges arising due to climate change.

The Botnar Research Centre for Child Health, in partnership with the University of Basel and ETH Zurich, aims to meet these health challenges. Timely preventive measures, robust diagnostics and adequate therapies can alleviate much of this disease burden. To realize these goals, we support the development and implementation of novel, accessible and sustainable healthcare solutions for young people who are most in need. BRCCH researchers are designing innovative biomedical tools and leveraging digital health technologies to address the unmet medical needs of the global paediatric population. Together with collaborators around the world, the BRCCH is striving to improve the health and well-being of young people.

Annual Report 2022
Botnar Research Centre for Child Health



BRCCH researchers and international collaborators use embryoid bodies as models for studying human diseases such as Fragile X Syndrome, the most common form of genetically inherited intellectual disability.
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

Once again, we pause at the end of a busy and dynamic year to reflect upon the recent activities at the BRCCH. The Centre has continued to drive innovation in paediatric global health by launching a new funding programme and has strengthened its community relationships at tailored events. While our research strategy evolved and adapted to new opportunities and needs, other aspects of our programme remained steadfast: our commitment to improving the health and well-being of young people worldwide and our vision to be a hub for excellence in paediatric biomedical research together with our partner institutions, the University of Basel, ETH Zurich, University Children's Hospital Basel (UKBB) and the Swiss and Tropical Public Health Institute (Swiss TPH).

This past spring, the BRCCH supported six consortia to pursue projects within its Principal Investigator Initiative (PII). Representing the fourth programme in the BRCCH's research portfolio, the PII provides key resources for international and multidisciplinary teams to develop and advance the implementation and uptake of step-changing innovations and intervention strategies with global reach, particularly those that can provide benefits for young people in low- and middle-income countries (LMICs). Together, 14 investigators from our partner institutions and 39 collaborators across 15 countries will aim to address challenges in paediatric infectious diseases and non-communicable conditions.

Successful international collaborations addressing the COVID-19 pandemic have reinforced the idea that working together is crucial to making a difference in the health and well-being of the vulnerable. Biomedical research progress can be rapid, step-changing and highly effective if researchers come together as a global community to share knowledge for a common purpose. Therefore, the BRCCH dedicated much of its efforts in 2022 to community-building, both locally in Switzerland and abroad. Bespoke events designed for BRCCH early career researchers provided learning opportunities in topics relevant to paediatric global health. Participants learned first-hand from global experts from the University of Oxford (UK), Stanford University (USA), the Commission for Research Partnerships with Developing Countries (Switzerland), the University of

Basel and NEO FOR NAMIBIA (Switzerland). The BRCCH also hosted public seminars ranging in topics from community-based healthcare, treatments tailored for paediatrics, malaria prevention and the paediatric microbiome. Across the seminars, 14 speakers from six countries and over 340 attendees from 26 countries gathered together to learn and share insights.

The Centre has benefited from constructive recommendations from external evaluators on how best to achieve its goals. Thus, the BRCCH was delighted to continue to work throughout 2022 with Fondation Botnar, the University of Basel and ETH Zurich on further shaping its strategic direction in the years to come. Notably, it looks forward to strengthening its research portfolio by launching the fifth component of its strategic plan, which will focus on professorships.

In this Annual Report for 2022, we are pleased to present further details of the year's research activities. We extend warm thanks for and recognition of the tireless work of BRCCH researchers, their teams and their international collaborators, despite a complex landscape of the continuing COVID-19 pandemic, military conflicts, energy shortages and economic stresses. We are very grateful for the engagement and collaboration of our partner institutions and we sincerely thank Fondation Botnar for their continued support and trust in us to fulfil our mission to improve the health and well-being of the most vulnerable around the world.

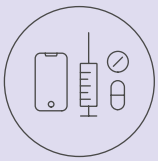
With our best wishes,

Georg Holländer

Sai Reddy

A Hub for Paediatric Research

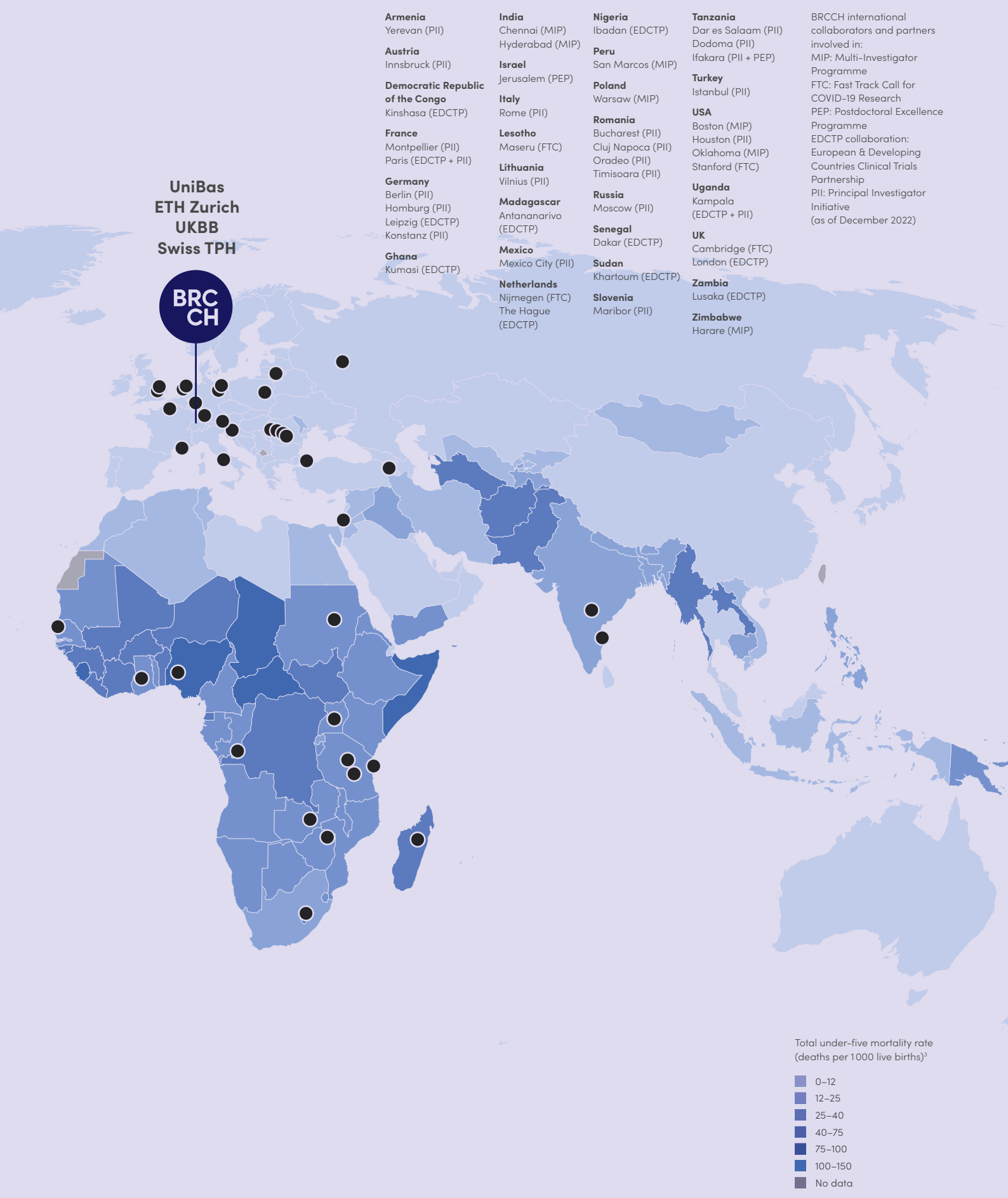
The BRCCH is based in Basel, Switzerland, and is generously supported by Fondation Botnar. BRCCH researchers at our four partner institutions – the University of Basel, ETH Zurich, University Children's Hospital Basel and the Swiss Tropical and Public Health Institute – form a strong community. National and international collaborators strengthen our network and together we are aligned in the common goal to improve child and adolescent health worldwide. In 2022, the BRCCH extended its global network and doubled its international research presence.



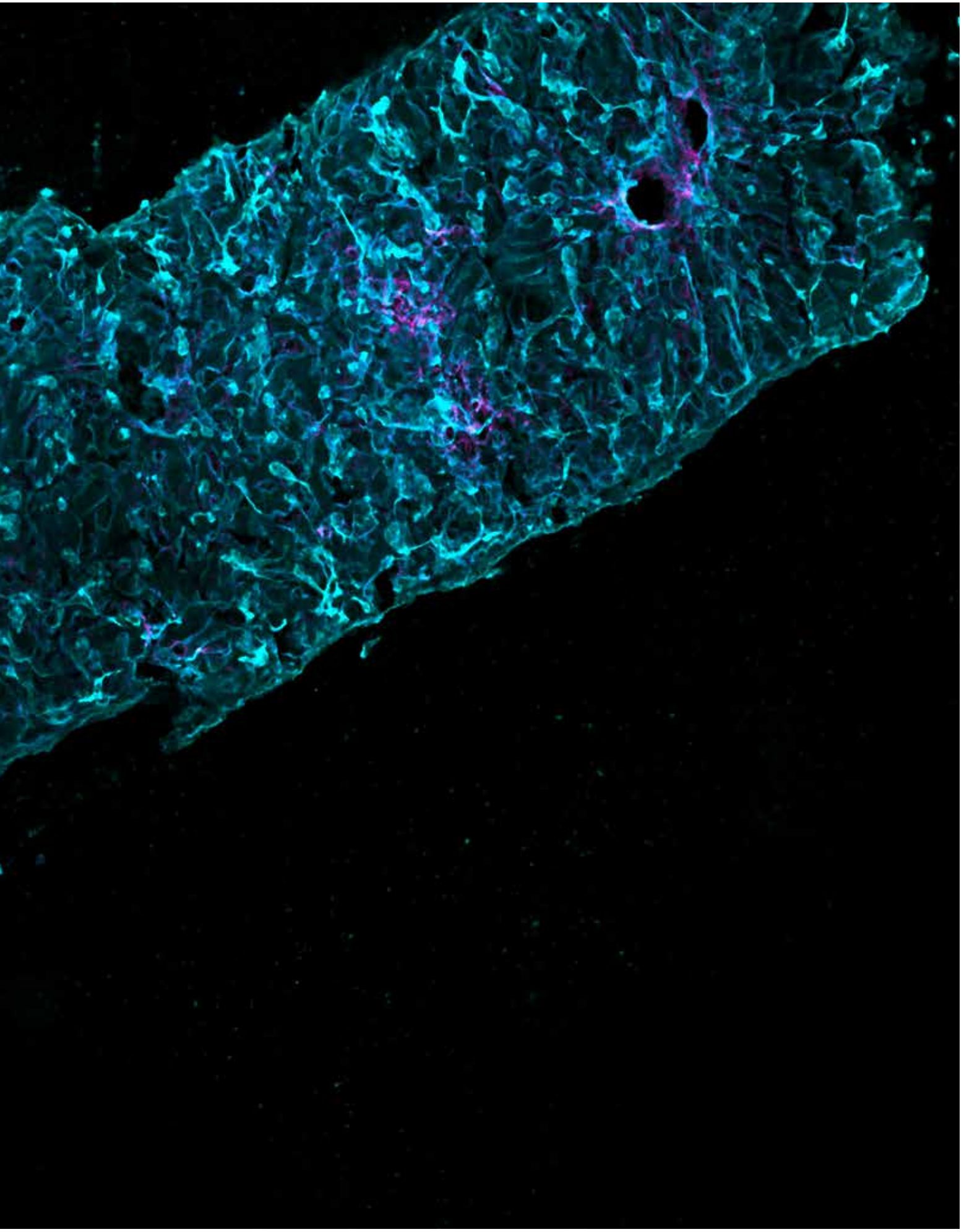
Our Mandate
is to drive outstanding and innovative scientific research that will lead to improved health outcomes and well-being in children and adolescents, particularly those in low- and middle-income countries.

Our Mission
is to embrace the expertise of our local and global partners and thus cultivate a research community and environment where new, effective and accessible paediatric healthcare solutions can emerge. To make this happen, multidisciplinary teams address unmet medical needs, implement innovative research and scale feasible solutions.

Our Vision
is to create a centre that fosters multidisciplinary and translational research in order to improve child and adolescent health through novel solutions for the prediction, diagnosis, treatment and prevention of disease. The BRCCH aims to become a crystallization point for national and international expertise in paediatric health.


UniBas
ETH Zurich
UKBB
Swiss TPH
BRC CH
Armenia
Yerevan (PII)
Austria
Innsbruck (PII)
Democratic Republic of the Congo
Kinshasa (EDCTP)
France
Montpellier (PII)
Paris (EDCTP + PII)
Germany
Berlin (PII)
Homburg (PII)
Leipzig (EDCTP)
Konstanz (PII)
Ghana
Kumasi (EDCTP)
India
Chennai (MIP)
Hyderabad (MIP)
Israel
Jerusalem (PEP)
Italy
Rome (PII)
Lesotho
Maseru (FTC)
Lithuania
Vilnius (PII)
Madagascar
Antananarivo (EDCTP)
Mexico
Mexico City (PII)
Netherlands
Nijmegen (FTC)
The Hague (EDCTP)
Nigeria
Ibadan (EDCTP)
Peru
San Marcos (MIP)
Poland
Warsaw (MIP)
Romania
Bucharest (PII)
Cluj Napoca (PII)
Oradeo (PII)
Timisoara (PII)
Russia
Moscow (PII)
Senegal
Dakar (EDCTP)
Sudan
Khartoum (EDCTP)
Slovenia
Maribor (PII)
Tanzania
Dar es Salaam (PII)
Dodoma (PII)
Ifakara (PII + PEP)
Turkey
Istanbul (PII)
USA
Boston (MIP)
Houston (PII)
Oklahoma (MIP)
Stanford (FTC)
Uganda
Kampala (EDCTP + PII)
UK
Cambridge (FTC)
London (EDCTP)
Zambia
Lusaka (EDCTP)
Zimbabwe
Harare (MIP)
BRCCH international collaborators and partners involved in:
MIP: Multi-Investigator Programme
FTC: Fast Track Call for COVID-19 Research
PEP: Postdoctoral Excellence Programme
EDCTP collaboration: European & Developing Countries Clinical Trials Partnership
PII: Principal Investigator Initiative
(as of December 2022)
Total under-five mortality rate (deaths per 1000 live births)[3]
0–12
12–25
25–40
40–75
75–100
100–150
No data

BRCCH researchers are studying the mechanisms of how protein interactions in the gastrointestinal system contribute to health on the cellular as well as the organ level. This image shows a murine liver cross-section. The tissue is stained with markers for cell nuclei (blue), fibronectin (cyan) and a tension sensor for fibronectin fibres (magenta). Studying mechanobiological tissue changes is highly informative and may lead to new therapeutic approaches in the future for diseases such as inflammatory or metabolic disorders. Credit: Ronja Rappold.



2022 in Review

April

Community-Based COVID-19 Testing in Lesotho and Zambia

Seminar – The BRCCH's first seminar of 2022 highlighted the collaborative project between Dr Klaus Reither (Swiss TPH) and Dr Kwame Shanaube (Zambart, Zambia), which aims to improve access to SARS-CoV-2 screening and testing. The seminar also featured insights from Dr Bulemba Katenda (Solidarmed, Lesotho), Dr Musonda Simwinga (Zambart, Zambia), and Moniek Bresser and Rahel Erhardt (both Swiss TPH), who are also working on this project. The speakers focused on the effects of community-led interventions in managing the COVID-19 epidemics in Lesotho and Zambia. In the picture below, a mother and child meet with a community healthcare worker at one of the project's mobile clinic sites in Lesotho (credit: MistraL and BRCCH). The clinic offers essential health services to members of the community in a setting where the provision of healthcare is fragile. This project is part of the joint initiative between the BRCCH and the European & Developing Countries Clinical Trials Partnership (EDCTP) to support multi-national collaborations for research to mitigate the impact of COVID-19 infections, particularly in LMICs. Further details about this project are on page 36. Participants located in nine countries across Europe, Africa, the Middle East and North America attended the online seminar.

"The course gave a nice overview and provided guidelines on how to approach an international collaboration, focusing on countries in the Global South. I think the principles presented will be especially useful."

"It was a great opportunity to interact with very informative speakers."

April

How to Establish Fair and Equitable Research Partnerships

Workshop – The BRCCH's Early Career Programme provides unique opportunities for its early career researchers to gain know-how in research areas that are at the heart of the Centre's mission and to grow their global network. Prof Jonas Karlström (SingHealth Duke-NUS Global Health Institute, Singapore) and Dr Fabian Käser (Commission for Research Partnerships with Developing Countries, Switzerland) presented a workshop on how to collaborate fairly and equitably in research. The participants learned about the key principles of cross-border research partnerships, analysed the application of the principles through a real-life case study and discussed how to implement effective collaborations in their own research. The workshop concluded with participants exchanging insights from their own experience during the networking session.

May

Principal Investigator Initiative

Launch – The BRCCH supported six new consortium-based projects within its Principal Investigator Initiative (PII) programme. The PII aims to drive interdisciplinary research that addresses critical challenges in global paediatric health and medicine. The call sought translational and cross-disciplinary research proposals that will deliver novel innovations across paediatric health diagnosis, disease treatment and prevention. The programme also welcomed projects that aim to advance the implementation and uptake of step-changing paediatric health interventions, particularly in LMICs. The BRCCH is proud to support the projects of lead investigators from our partner institutions: Dr Marc Birkhölzer (University of Basel), Prof Philippe Claude Cattin (University of Basel), Prof Edgar Delgado-Eckert (UKBB), Prof Elgar Fleisch (ETH Zurich), Prof Jennifer Keiser (Swiss TPH), Dr Sarah Moore (Swiss TPH), Prof Daniel Paris (Swiss TPH), Prof Marc Pfister (UKBB), Prof Amanda Ross (Swiss TPH), Prof Torsten Schmitz Cherdron (Swiss TPH), Prof Peter Steinmann (Swiss TPH), Prof Gabor Szinnai (UKBB), Prof Fabrizio Tediosi (Swiss TPH) and Prof Janos Vörös (ETH Zurich). Each project is supported with up to 1 million CHF. Over the next four years, these BRCCH researchers, in partnership with 38 international collaborators across 15 countries, will drive ambitious projects across diagnostics, therapeutics, digital health and public health to combat a range of diseases afflicting children and adolescents worldwide. More information about the PII is on pages 43–49. Credit: Ground Picture.

May

Understanding Key Challenges of Global Paediatric Health

Lecture – Global expert Prof Yvonne Maldonado (Stanford University, USA) spoke to BRCCH researchers about the state of the field of paediatric research during a BRCCH Early Career Programme event. She has extensively studied viral diseases such as polio, measles and ebola around the world. Her work on mother-to-child transmission of HIV in sub-Saharan Africa is credited with preventing hundreds of thousands of babies from acquiring HIV. During her lecture, participants learned about the particularities and challenges of conducting translational research in paediatric health. Prof Maldonado offered perspective on the current status and biggest medical gaps in paediatric health today across high-, middle- and low-income countries. Image: *Streptococcus pneumoniae* is the most common causative agent of pneumonia. This infection, along with other lower respiratory diseases, has been the leading cause of death worldwide in children under five in recent years[1]. Thus, these infections represent an unmet health challenge in young people. Credit: Jennifer Oosthuizen/ CDC.

May

Impact of COVID-19 on Global Paediatric Health

Roundtable discussion – Paediatric experts gathered in Basel to discuss how the COVID-19 pandemic has affected global paediatric health. Prof Julia Dratva (Head of the Public Health Research Unit at the Zürich University of Applied Sciences, Switzerland, and an assistant professor at the University of Basel) moderated a panel discussion with:

- Prof Yvonne Maldonado (Professor of Paediatrics, Epidemiology and Population Health and Chief of the Division of Paediatric Infectious Diseases, School of Medicine, Stanford University, USA)
- Prof Alan Stein (Professor of Child and Adolescent Psychiatry, University of Oxford, UK)
- Dr Marc Birkhölzer (Psychiatrist, University of Basel and BRCCH PII lead reseacher)
- Prof Thomas Berger (Specialist in Neonatology and Secretary and Chief Medical Advisor at NEO FOR NAMIBIA, Switzerland)

The experts highlighted several important consequences of the pandemic for young people, including:

- decreased access to vital child healthcare services such as neonatal care and immunization
- increased poverty
- more widespread nutritional deprivation and decreased physical activity
- increased strain on mental health
- loss of a caregiver
- compromised learning opportunities

Credit: Soumyabrata Roy.

July

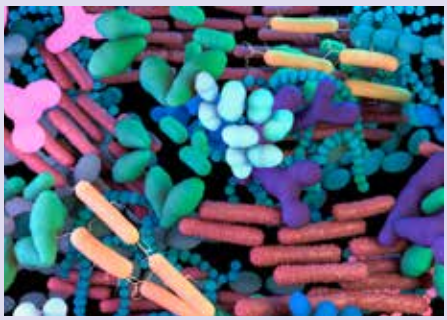
Refining Paediatric Treatments for All

Seminar – This hybrid event highlighted the research of three keynote speakers. The first speaker, Prof Thomas Erb (UKBB), leads the "COVent: Improve Ventilation Safety by Means of Intra-Tracheal Pressure Monitoring – A Short-Term Solution" project within the BRCCH's Fast Track Call for COVID-19 Research programme. Here, he presented his work improving the safety of children undergoing anaesthesia and sedation and the challenges in taking up and adopting innovative paediatric medical devices in clinical practice. This research is detailed on page 22. Next, Dr Marianne Schmid Daners (ETH Zurich) provided an overview of her research on the dynamics of the intracranial system. She highlighted her work to develop a biomedical device for the control and treatment of hydrocephalus. Finally, Prof Kokila Lakhoo (University of Oxford, UK) presented her work on providing surgical treatments to children in need in LMICs. She concluded her talk by emphasizing that it is important to work towards equity in healthcare provision in order to achieve justice around the world. The seminar was attended both in person and remotely by participants from countries across Europe, the Middle East and North America. Image: A tiny pressure sensor measures only 750 µm × 220 µm × 75 µm. This device may enable healthcare workers to monitor intra-tracheal pressure while patients are being ventilated. Credit: AMSYS:TE Connectivity.

October

Malaria Prevention: Progress and Prospects

Seminar – Three keynote speakers discussed their research on malaria in a meeting that adopted a hybrid format. Prof Simon Draper (University of Oxford, UK) highlighted the challenges, cutting-edge developments, successes and future of vaccine-based solutions to malaria. Prof Melissa Penny (Swiss TPH) shared her work on harnessing complex data and computational models to evaluate and predict malaria disease dynamics and advance the design of novel intervention strategies for malaria prevention. Prof Evelyn Korkor Ansah (University of Health and Allied Sciences, Ghana) provided deep insights into her work to manage malaria at the community level in Ghana. She highlighted the pressing need for tailored, multi-level intervention strategies to ensure that no one gets left behind. Participants from 17 countries attended the seminar online and in person. Prof Penny also leads the "Using Model-Based Evidence to Optimize Medical Intervention Profiles and Disease Management Strategies for COVID-19 Control" research project at the BRCCH within the Fast Track Call for COVID-19 Research programme (see page 26). Image: One potential way to help prevent malaria infection in humans is to reduce the parasite burden in female *Anopheles* mosquitos. Credit: Nechaevkon.



November

Importance of Microbiota in Paediatric Health

Seminar – In the final seminar of the year, two experts focused on the gut microbiome (visualized in a 3D rendering above; credit: Design Cells) in young children. Prof Emma Slack (ETH Zurich) presented the latest progress of her BRCCH project entitled "Precision Microbiota Engineering for Child Health." She spoke about the potential to engineer the microbiome in the intestinal tract as a way to address inborn errors of metabolism and neonatal sepsis. She also highlighted recent research results that indicate that an adult-like microbiome positively influences the health of an animal model with a mild urea cycle disorder, a type of inborn error of metabolism. Prof Mathias Hornef (University Hospital Aachen, Germany) presented his work exploring how the microbiome establishes itself in neonates. An interesting aspect is that the neonatal microbiome can be modified and thus introduced probiotic bacteria can exert a beneficial effect; for example, for preventing necrotizing enterocolitis. Participants from nine countries across Africa, Europe and North America joined the seminar online and in person. Prof Slack's project is part of the BRCCH's Multi-Investigator Programme (MIP) (see page 20).

December

Snapshots by Early Career Researchers

Images: Researchers participated in the second edition of the BRCCH Image Contest for early career researchers. The entries reflect the work and activities of BRCCH projects over the past year. Judged for alignment with the BRCCH's scientific scope and aesthetics, the winners were awarded sponsorship to participate in a scientific congress of their choice in 2023.

Our congratulations to:
Dr Marta S Palmeirim, PII researcher: Her image, below, shows a glimpse into a cross-sectional study conducted by her and her colleagues in the Kibaoni ward in Tanzania. Research assistants collected samples from participating children to check for different parasitic diseases such as soil-transmitted helminthiasis, schistosomiasis, intestinal protozoa infections, malaria and lymphatic filariasis. Dr Palmeirim is a researcher in a BRCCH project that is doing similar research in Uganda to study a combination drug treatment against soil-transmitted helminths. The project and consortium are further detailed on page 46. Credit: M.S. Palmeirim.

Dr Prasad Nalabothu, MIP researcher: In his image, he and a mother check the fit of an orthopaedic palatal plate in her baby to treat the baby's cleft lip and palate until surgery can be safely performed. During his research visit to the project's partner, the Cleft and Craniofacial Centre at Saveetha Medical College and Hospital in Chennai, India, Dr Nalabothu and colleagues applied a digital workflow involving artificial intelligence to produce the palatal plate using a 3D printer. This process was developed by the MIP consortium and achieved the project's early milestone of adoption outside of Switzerland. Further details about the project and the image are featured on page 18. Credit: P. Nalabothu and Dr Praveen Ganesh.

Dr Keith Gunapala, PEP fellow: His image shows a mass of human embryonic stem cells that form *in vitro* and develop some of the organizational and molecular properties of organs, i.e., an organ pre-cursor in a petri dish. These so-called embryoid bodies are useful models for studying human diseases and investigating potential therapeutic approaches. Further project details can be found on page 40. The image is featured on page 1. Credit: Nissim Benvenisty Lab, Azrieli Center for Stem Cells and Genetic Research, Hebrew University of Jerusalem.

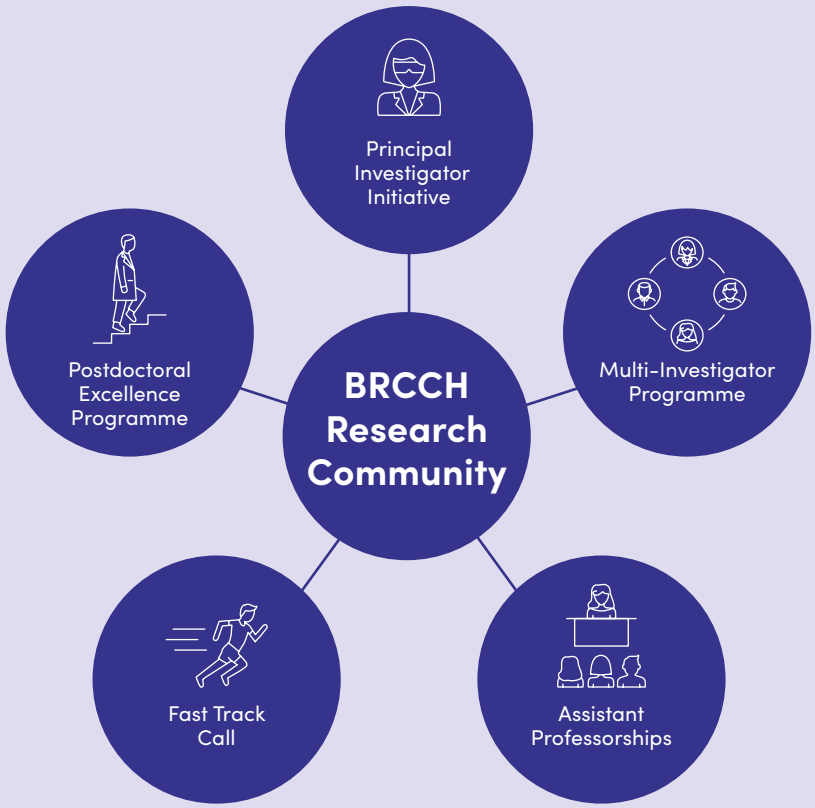
Reflecting on the first Image Contest: We thank 2021's entrants and we hope that the winners have benefited from their congress attendance.

Ronja Rappold (MIP PhD student) attended the 2022 EMBL Symposium on Mechanobiology in Development and Disease in Heidelberg, Germany.

Dr Michele Gregorini (FTC researcher) took part in the 18th Münchner AIDS- und COVID-Tage in Munich, Germany.

Dr Keith Gunapala (PEP fellow) participated in the International Society for Stem Cell Research (ISSCR) 2022 Annual Meeting in San Francisco, USA.

Here is What to Look Forward to in 2023



Strategy
The BRCCH's funding programmes will continue to support cutting-edge research aiming to develop and implement innovative, accessible and sustainable healthcare solutions for young people across all age groups. With the successful take-offs of four funding programmes so far, the BRCCH is now particularly looking ahead to the launch of the final component of its research strategy: the establishment of professorships.

Assistant Professorships
In the upcoming years, the BRCCH aims to facilitate the creation of professorships at the University of Basel and ETH Zurich. The research activities of these professorships will be fully dedicated to the global advancement of young people's health. The professors and their research groups will be located in Basel and will be embedded in a vibrant research environment offering unique opportunities for collaboration.

Thus, the BRCCH aims to foster a synergistic cluster of expertise that will pioneer novel, data-driven approaches to understanding and responding to challenges in young people's health. This cluster will also nurture the next generation of scientists to become proficient in tackling significant (global) paediatric health problems. Moreover, it will drive the development of innovative tools and methodologies to advance paediatric medical interventions and policies, thus creating a long-term impact on the health and well-being of young people worldwide both at the individual and population levels.

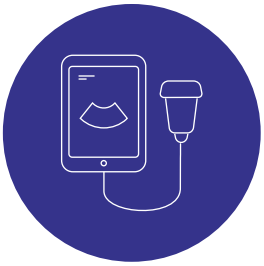
The first milestone in the realization of this cluster was achieved with the planned profile for a professorship in Paediatric Digital Health Data and Analytics, which is expected to develop novel approaches to advance big health data analytics for use in paediatric medicine. The position was approved by the University Council as part of the University of Basel's development and structural plan.

Community
The BRCCH continues to strengthen its community through activities that complement its funding programmes. These efforts towards disseminating knowledge and fostering synergies come from the BRCCH's capacity-building. To this end, BRCCH researchers communicate their progress, learning and achievements. Novel research in paediatric health is highlighted and speakers are invited to share their cutting-edge expertise to further strengthen the BRCCH's collective know-how. The BRCCH's future research building will also facilitate community-building.

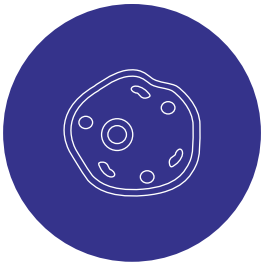
Research Building
From 2025 onwards, the BRCCH will enjoy the benefits of a central research location at the so-called Basel *Schällemätteli* campus. The brand-new building, which will be constructed with ecological considerations in mind, will become the joint home of the BRCCH's professors and their research groups, with the majority focusing on *in silico* research relevant to the Centre's scope. The close proximity to UKBB, ETH Zurich's Department of Biosystems Science and Engineering, the Life Science Cluster of the University of Basel and the nearby Swiss TPH will enable the ideal conditions for collaboration and allow BRCCH researchers to access pre-existing research infrastructure. The BRCCH's vision is that this site will foster innovative paediatric research and that it will welcome research and translational partners from around the globe. Credit: Guerra Clauss Garin Architekten.

Strategy

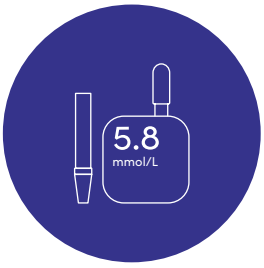
The BRCCH and its partners are conducting multi-disciplinary research projects that address unmet medical needs across a wide range of communicable and non-communicable conditions affecting young people around the globe. The BRCCH's research goals are to predict, prevent, treat and – where possible – cure diseases in children and adolescents worldwide. The Centre's project portfolio covers four research areas in order to achieve these ambitious goals.



Paediatric Digital Health
Using digital tools specifically tailored to the needs of young people, the BRCCH seeks to improve effective disease modelling, diagnosis, treatment and monitoring.



Advanced Bioengineering for Paediatric Medicine
The BRCCH aims to support bioengineering-based innovations in precision medicine specific to paediatrics and to foster their application to health challenges in young people.

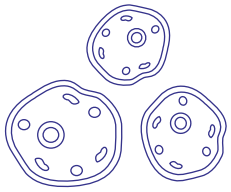


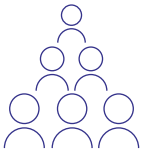
Essential Paediatric Medical Devices
The BRCCH supports the cutting-edge design of essential, age-appropriate medical devices that meet the criteria to be used both in young people and under conditions relevant to LMICs.

Ethics, Policy and Implementation Research in Paediatric Health
The BRCCH focuses on research especially tailored to paediatrics in terms of ethics, policy and implementation strategies for application to paediatric health interventions.

Research Portfolio

The BRCCH supports a comprehensive project portfolio comprising research spanning from early-stage innovation development to research focused on technology validation and implementation. This pipeline ensures that the Centre will deliver on its ambitious goals.



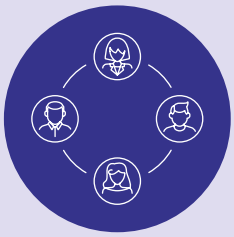


Cellular Systems — Population

Early-Stage Projects
have significant potential for innovation and a long-term vision for translation and implementation in high-, middle- and/or low-income countries. These projects address relevant challenges associated with high disease burden and/or societal impact in LMICs. The BRCCH therefore enables scientifically outstanding early-stage research that promises to deliver step-changing solutions.

Translational Projects
are on the path to implementation and are at a point where prior research findings now merit further validation at scale and translation into use-inspired solutions. Translational projects advance early technology and engineering developments designed to improve diagnostics, disease monitoring and/or therapy. This segment of the BRCCH's portfolio represents an important stepping stone towards validating early-stage innovations in clinical and public health settings.

Mature-Stage Projects
test the feasibility, robustness and usefulness of technologies and methods for disease diagnosis, treatment, monitoring and prediction on a larger scale, in real-world context-dependent settings. These projects aim to facilitate the successful uptake of new intervention strategies for young people in the future, especially in resource-limited settings.



Multi-Investigator Programme

The Multi-Investigator Programme (MIP) encompasses projects that form the cornerstones of the BRCCH's research portfolio. This programme supports multidisciplinary partnerships among researchers from our four partner institutions and their international collaborators leading groundbreaking research across biodiagnostics, therapeutic bioengineering and digital health-based intervention strategies.

Four ambitious projects are currently supported by the MIP initiative. Thirteen lead researchers and 19 collaborators from six countries began their activities in early 2020 and will continue their research for five years.

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

Overview: Families living in remote areas, especially those in LMICs, 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. Researchers will assess the effectiveness and improve the performance of an interactive mobile phone-based application using artificial intelligence. The aim is to further develop this digital tool in order to help parents to best support their children's development in the first 1,000 days of life.

Update: In 2022, the consortium focused on recruiting families and their young children in the San Marcos, Cajabamba and Cajamarca regions of Peru to be involved in their study, with the long-term aim of involving more than 2,000 families in total. As part of their study, more than 1,000 families have been receiving parenting support through the app. In a control group setting, the researchers trained local field staff in conducting home visits, which were delivered bi-weekly to 270 families in 2022. Following the loosening of COVID-19 restrictions in Peru, the consortium also took the opportunity to successfully engage with key local stakeholders, including provincial district authorities and implementers of childhood development programmes, to pave a path towards creating long-term impacts for local children and their families. Finally, the consortium further improved the Afinidata® digital platform's resources by including the most suitable smartphone-based activities for children in the coming year.

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 during their children's early development. 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: At present, there are no effective preventive measures for cleft lip and palate, the most frequent craniofacial malformation in newborns. Researchers working on this project aim to develop a smartphone image-based method for computing a 3D image of the cleft. This innovative method will enable three new treatment regimes: 1) a quantifiable correlation between the cleft shape, the optimal time point for surgical intervention and its outcome; 2) a fully automated digital fabrication of individualized orthopaedic palatal plates that will help to reduce the size of the cleft before surgery and 3) the closure of the cleft in a single surgery instead of multiple procedures.

Update: In 2022, the project achieved a major milestone: the computation of the digital palatal plate based on an intraoral scan. The team successfully integrated the technology into the clinical workflows at University Hospital Basel and also successfully transferred it to partner clinics in India. To date, 19 young patients in Switzerland and India have been treated with plates computed with the fully digital pipeline that uses artificial intelligence, automation and decentralized 3D printing. The digital workflow is available open access in order to facilitate knowledge uptake and capacity-building. Researchers also improved their methods in 3D geometry acquisition, using smartphone videos to produce accurate 3D reconstructions. Future work will make this part of the pipeline more robust, enabling the generation of palatal plates based on smartphone inputs, which represents a low-cost solution for healthcare centres in low-income countries.

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, Zürich); Syed Altaf Hussain (Sri Ramachandra Institute of Higher Education and Research, India); RVM Surya Rao (Saveetha Medical College and Hospital, India).

Image: Dr Prasad Nalabothu and a mother check that an orthopaedic plate is sitting correctly in her baby's mouth. Credit: P. Nalabothu and Dr Praveen Ganesh.

Lead Researchers

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 do not reach their developmental potential each year, which is predominantly due to infectious diseases, malnutrition and related disorders. Illness or disease in the body may trigger changes in the microbiota in the gastrointestinal tract, or gut. 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: The consortium focused on characterizing the engineered bacteria in controlled laboratory settings to better understand 1) what precisely the engineered bacteria can sense and report on when inside the gut and 2) whether they are able to detect different conditions in the gut and how this changes over time. By studying how these engineered bacteria behave in animal models, the researchers made breakthrough discoveries by demonstrating that they pass safely through the gut and that they are indeed able to detect and record changes in the gut as a measure of health status in mice. Furthermore, the consortium invested strong efforts in collecting longitudinal biological samples from mothers and babies living in Zimbabwe and Switzerland to enable future investigation into how malnutrition and related disorders affect gut functions in children in different settings.

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

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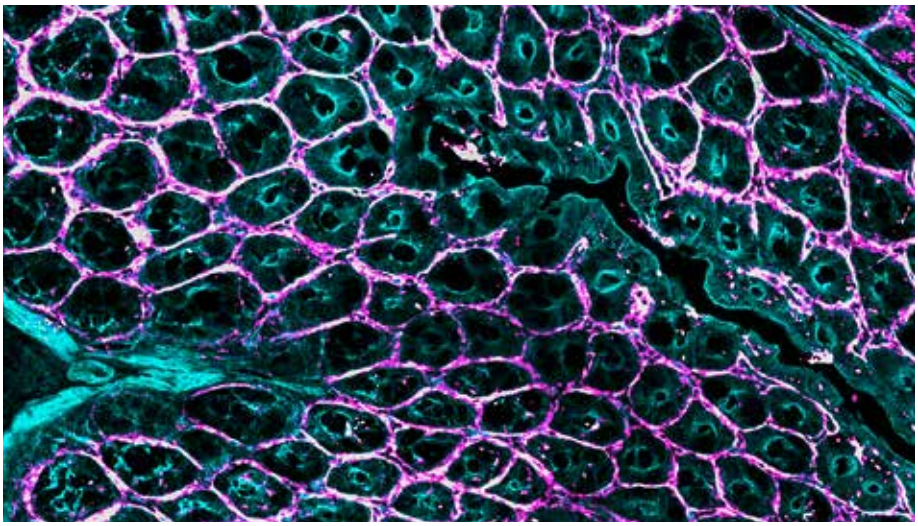

Precision Microbiota Engineering for Child Health

Overview: From shortly after birth, a baby's large intestine is colonized by billions of bacteria with major consequences for child health and development. Current research supports the idea that the microbiome has a causal role in conditions as diverse as allergies and autism. Despite this, we still lack accurate medical interventions to "fix" the microbiota. This project aims to develop precise tools that work with intestinal physiology to alter the metabolism of the gut microbiota or to replace "bad" bacteria with "desirable" ones. Its researchers are targeting two catastrophic neonatal diseases: *E. coli*-driven neonatal sepsis and inborn errors of metabolism. Overall, the research will generate fundamental insights into microbiota, as well as preclinical insights into therapy efficacy and safety.

Update: The consortium is conducting two studies in order to identify relevant targets for microbiota engineering techniques in human patients, with clinical sample collection 80% complete. In parallel, the researchers are continuing to advance microbiota engineering tools and accompanying diagnostics. In mouse models, they have successfully established tools and protocols to eliminate pathogenic *E. coli* presence in adult mice and to suppress maternal transmission of the bacteria to mouse neonates, with broad implications for preventing neonatal infections. The project has also identified a link between circadian rhythm and microbiota-driven effects on host metabolism and uncovered a strong protective effect of a pathogen-free microbiome in a mouse model of a urea cycle disorder. Their findings confirm the relevance of targeted microbiota engineering to benefit patients. Going forward, the project will bring the clinical studies and the microbiota engineering technology together to develop patient-targeted therapies and diagnostics, ready to move into clinical testing.

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

Image: A 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

In a rapid response to the emerging COVID-19 pandemic, the BRCCH launched a Fast Track Call (FTC) for Acute Global Health Challenges, which was made possible by additional and generous financial resources from Fondation Botnar. The FTC's objectives were to quickly enable research that will help to immediately mitigate medical and public health challenges presented by the pandemic in the short term and to contribute to tangible solutions that will lead to better preparedness and reduced global disease burden in the future.

By May 2020, 11 research consortia involving 32 lead researchers and 41 collaborators from five countries had been awarded support for projects in the areas of COVID-19 immunology, diagnostics, medical interventions and disease management.

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

Overview: A frequent cause of critical illness and mortality in severe COVID-19 cases is acute respiratory distress syndrome (ARDS). 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. Specifically, it aims to incorporate a sensor into the ventilator to monitor and control pressure in the trachea.

Update: In 2022, the researchers completed *in vitro* work to integrate a novel pressure sensor into a low-cost ventilator. They also adapted an add-on system for the sensor to be situated at the end of the endotracheal tube. The pressure sensor was harmonized into the ventilator hardware and software and the ventilator control was adjusted to control the intratracheal pressure. Further studies addressing the influence of airway resistance on intratracheal pressure were conducted on the low-cost ventilator test system. The findings of the *in vitro* experiments were analysed, documented and submitted for publication. The researchers will continue their progress with their plans for *in vivo* trials, which are currently under preparation and will be conducted in 2023.

Collaborators: Nicolas Glaser, Frederic Zanella (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

Thomas Erb
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Jürg Hammer
University Children's Hospital Basel

Mirko Meboldt
ETH Zurich

Marianne Schmid Daners
ETH Zurich

ISINC-19: Immune Senescence in COVID-19

Overview: SARS-CoV-2 continues to infect people, and it is still unclear why some individuals develop severe illness while others develop only mild or even no symptoms. This 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: By investigating plasma concentration trajectories of the inflammatory marker C-reactive protein (CRP), the consortium discovered that COVID-19 patients can be grouped into three categories: 1) patients with absent or mild inflammation; 2) patients with early, resolving inflammation or 3) patients with persisting inflammation. Uniquely, the consortium determined that COVID-19 patients with persisting inflammation exhibit greater perturbations in an immunomodulatory metabolic pathway, known as the kynurenine pathway, and that the deregulation of this pathway is linked to a prolonged abundance of inflammatory cytokines in the blood. Furthermore, the researchers investigated the effects of repurposed drugs that impact mitochondrial function in immune cells known as B cells during inflammation. This led to the identification of promising drug candidates that will be investigated as future potential therapeutic strategies for COVID-19 patients.

Collaborators: Daiana Stolz (University Hospital Basel), Hélène Ruffieux (University of Cambridge, UK).

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 and University of Cambridge, UK

Glenn Bantug
University of Basel

Christoph Berger
University Hospital Basel

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

Overview: This project aims to understand the adaptive immune responses that follow infection with SARS-CoV-2 and to delineate the influence of mild or severe infection and vaccination on the immune system. The consortium focuses on studying two immune cell types: CD8+ T cells, which kill virus-infected cells, and B cells, which produce antibodies that neutralize infective viral particles. They combine innovative approaches in high-throughput testing of SARS-CoV-2 peptides, immune receptor analysis and related antigen-affinity assays in order to interrogate the immune repertoire of COVID-19 patients and to understand how long-lived immunity to SARS-CoV-2 is shaped.

Update: The consortium generated phenotypic and transcriptomic profiles of SARS-CoV-2-specific T cells from COVID-19 patients and collected longitudinal datasets that followed these patients for up to 12 months after infection. By mapping out how T cell responses are shaped following SARS-CoV-2 infection, their work revealed that memory formation in CD8+ T cells is regulated by a balance of different immune signalling mechanisms during acute infection. This subset of long-lived T cells, known as memory T cells, were found to circulate in the blood and to contribute to long-term protection against COVID-19. The consortium also utilized these approaches to map memory formation in B cells during SARS-CoV-2 infection and after vaccination. This revealed that SARS-CoV-2-specific memory B cells can have different fates with distinct cellular functions and that these B cells can change fate following vaccination after natural infection. Taken together, the consortium's work has significantly contributed to understanding the development and plasticity of adaptive immune responses following SARS-CoV-2 infection and vaccination. The consortium hopes that these results will inform future vaccine strategies and, in the wider context, contribute to understanding how robust and long-term immunity is formed against different pathogens.

Collaborators: Randall Platt (ETH Zurich); Onur Boyman, Sarah Adamo, Yves Zurbuchen (University of Zürich).

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

Lead Researchers

Andreas Moor
ETH Zurich

Yakir Guri
University Hospital Basel

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

Overview: Researchers are developing a novel COVID-19 rapid diagnostic test (RDT) based on saliva for self-testing at home. The DAVINCI RDT can detect antigens of and antibodies against the 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 quickly evaluate their own individual immune status, 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 successfully developed a prototype rapid test for COVID-19 antigens and immunity. This prototype represents the first platform of a saliva-based test intended for home use without the need for any sample preparation or additional reagents. The user spits into the test device and gets a visual result after 12 minutes (i.e., test lines). In addition and as an add-on option, the test results can be scanned with a smartphone-based application developed by the consortium. The app analyses the resulting test lines, provides an interpretation of the result, registers the user and archives past results, which enables the user to track results over time and facilitates future integration into e-health systems. This prototype of a simple, rapid test for home use is the fundamental basis for a technology platform that can lead to the future further development and application of the device for the analysis of various diseases in saliva specimens.

Collaborators: Philip Howes, Monika Colombo (ETH Zurich); Frank Dieterle (Swiss TPH); Samantha Paoletti (CSEM); Peter Spies (FHNW); Vanja Ivancevic, Pascal Winnen (HEMEX); Christoph Schäfer (BioInitials); Nila-Pia Rähle (Effectum Medical).

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
Swiss TPH

Daniel Richards
ETH Zurich

Stefan Stübinger
University of Basel

Miodrag Savic
University Hospital Basel

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 harnesses 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 contribute scientific insights 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 to examine 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 are investigating the future effects of long-term vaccination strategies, immunization rates and novel COVID-19 medical interventions.

Collaborators: Sherrie Kelly, Epke Le Rutte (Swiss TPH); Sarah Kadelka, Judith Bouman (ETH Zurich).

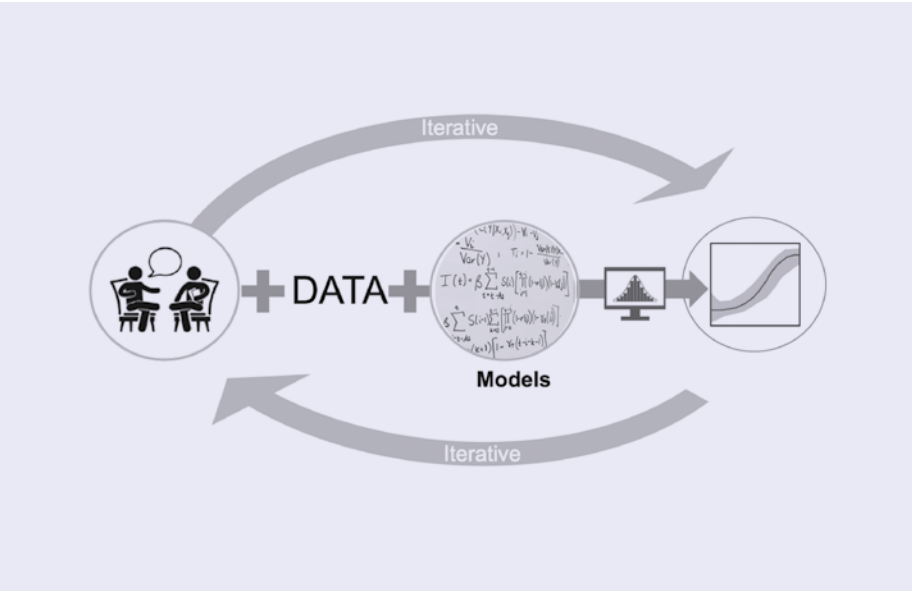


Image: Modelling support is an iterative process that uses available data to generate predictions for use in decision-making. Mathematical modelling can help with prioritization and investment in novel medical tools for COVID-19. Credit: Melissa Penny.

Lead Researchers

Melissa Penny
Swiss TPH

Andrew Shattock
Swiss TPH

Nakul Chitnis
Swiss TPH

Roland Regoes
ETH Zurich

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

Overview: CRISPR-based technology may enable researchers to identify crucial factors for SARS-CoV-2 to infect and cause disease in humans. This consortium is using a combination of *in vitro*- and *in vivo*-based strategies 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: Recent evidence indicates that host genetics can alter individual susceptibility to SARS-CoV-2 infection. However, the genetic elements that are responsible for this and how patient-specific genetic mutations may influence infection susceptibility are largely unknown. Therefore, this year, the consortium focused on developing a novel gene-editing strategy involving base and prime editing technologies to answer these questions. This strategy enabled the researchers to assess the pathogenicity of thousands of short genetic mutations in parallel and to perform proof-of-concept studies using human cells. This work will allow the consortium to link specific genetic variants to different cellular and clinical phenotypes observed following SARS-CoV-2 infection. In the future, these tools could also be used to understand the influence of genetic variation on individual health outcomes in a variety of diseases.

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

Lead Researchers

Randall Platt
ETH Zurich

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

Overview: Two central challenges in mitigating the COVID-19 pandemic are the difficulty of detecting infection and the emergence of mutated variant strains of SARS-CoV-2. 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. First, it 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: In 2022, the project made significant progress in identifying and predicting future variants of SARS-CoV-2. The researchers developed deep mutational learning (DML), a machine learning-guided protein engineering technology that interrogates combinatorial mutations in the receptor-binding domain (RBD) of SARS-CoV-2 for their impact on cellular infection and antibody escape. DML can thus provide information on how a new variant may affect vaccinated or previously infected people, potentially in real time as the variant emerges in a population. The team focused on applying DML methods in order to understand Omicron-based RBD variants. Importantly, the researchers took the project a step further along the innovation pipeline by forging new collaborations with a biotechnology company and an international research group in order to use DML to help screen antibodies and predict escape by virus variants, and thus potentially guide the selection of future antibody therapeutics for SARS-CoV-2 infection.

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

Lead Researchers

Sai Reddy
ETH Zurich

Yakir Guri
University Hospital Basel

Michael Nash
University of Basel

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

Overview: Mitigation strategies against COVID-19 must be context-specific and take local conditions into account in order to be effective and efficient. Limited resources and fragile healthcare systems often dictate what is feasible in low- and lower-middle-income countries. In this project, researchers are combining artificial intelligence, portable chest X-ray machines and antigen-based rapid diagnostic tests (RDTs) in order to enable and improve the diagnosis of COVID-19 patients and ensure that essential health services are provided in settings with limited resources.

Update: In 2022, the consortium concluded research activities in rural Lesotho, screening nearly 180,000 adults and children for COVID-19/tuberculosis (TB) symptoms or recent exposure to COVID-19. More than half of those who were screened positive were enrolled in an integrated TB/COVID-19/HIV project. The team evaluated the diagnostic performance of an artificial intelligence software tool (CAD4COVID) for radiographs. They found that a combination of CAD4COVID analysis and white blood cell count had comparable diagnostic performance to that of RDTs. Nasal sampling appeared to be a good alternative to nasopharyngeal sampling for the RDT. In a proof-of-concept study, they demonstrated for the first time that SARS-CoV-2 can be detected with a simple bioaerosol collection device. Overall, the project developed a model of care for community-based screening, triage and essential health services suitable even for remote areas of Lesotho.

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 health clinic, a health worker takes a chest x-ray of a child with COVID-19-like symptoms. The image is then assessed using AI software to estimate the probability of the presence of COVID-19 pneumonia or TB. Credit: MistraL and BRCCH.

Lead Researchers

Klaus Reither
Swiss TPH

Niklaus Labhardt
University Hospital Basel

peakPCR: Making DNA Analyses Faster and More Accessible

Overview: 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 LMIC settings.

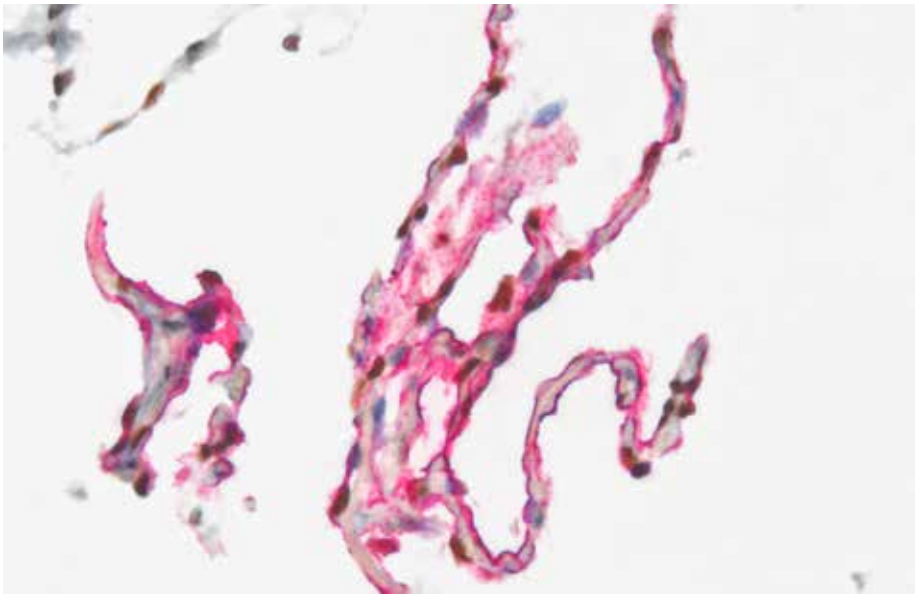
Update: The project has led to the development of a radically new rapid PCR testing platform that can quickly detect several viral and bacterial pathogens with high reliability and at an accessible price. The consortium succeeded in performing extensive validation of the platform in more than 15 countries across Europe, Africa and South America, involving over 10,000 tests. The researchers invested significant efforts into improving the system in order to reduce the hands-on time for users and increase robustness against uncertainties related to the global supply chain crisis. Furthermore, this year, they obtained CE marking, which will allow the platform to be made available in the form of a medical device. The consortium aspires for peakPCR to offer the most accessible, high-quality PCR tests for a variety of infectious diseases suitable for use in resource-limited settings and beyond.

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



Lessons from the Deceased to the Living and Back

Overview: Initially, 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 "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" 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: Over the past year, the consortium has made critical contributions to understanding the effects of COVID-19 on different parts of the body. Firstly, the researchers demonstrated that the cardiac effects of COVID-19 are angiocentric, macrophage-driven inflammatory processes that are distinct from other antiviral inflammatory responses. Importantly, based on pathology and clinical data, they identified structural heart disease as a distinct risk factor for severe COVID-19. Interestingly, the consortium also discovered that SARS-CoV-2 can infect and replicate in fat tissue, where it can induce systemic inflammation that leads to severe COVID-19. Finally, concerning the neurological effects of COVID-19 – coined as ''Neuro-COVID'' – the consortium identified that the most prominent signs of severe Neuro-COVID are blood-brain barrier impairment, structural changes in the brain, microglia activation and abnormal inflammatory immune responses.

Collaborators: Colleagues at University Hospital Basel; Cantonal Hospital Liestal, Switzerland; Stanford University, USA; Harvard University, USA.

Image: COVID-19 affects the blood vessels. A 400x magnified view of the alveolar septum using immunohistochemistry shows SARS-CoV-2 N-protein (in red) in proximity to endothelial cells (ERG positive, in brown), indicative of the prominent role of blood vessels in the pathophysiology of COVID-19. Credit: Jasmin Dionne Haslbauer.

Lead Researchers

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

Overview: The incubation period for SARS-CoV-2 lasts several days, during which time patients do not experience any symptoms. This period represents a blind spot in public health: many people may be infectious, but 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 consortium is developing such a diagnostic test based on lateral flow assays that will optimize the sensitivity and precision of COVID-19 testing.

Update: The consortium has successfully established a production line for its novel SARS-CoV-2 rapid antigen tests. It developed a fully automated version of the readout device's interface module to enhance usability and improved the device's software and error handling. Consequently, these antigen tests offer a better limit of detection and quantitative readout than SARS-CoV-2 tests currently available on the market. Finally, the researchers succeeded in deploying 240 rapid antigen tests together with readout devices in University Hospital Basel for clinical validation studies. In the coming year, they aim to complete clinical testing and to establish an upscalable manufacturing process to support future real-world applications of their innovative technology.

Collaborators: Alexander Tanno (ETH Zurich and Hemetron AG); Noé Brasier (University Hospital Basel).

Image: The consortium is working to create a rapid point-of-need diagnostic test. A sample droplet is loaded onto the sample pad 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.

BRCCH-EDCTP COVID-19 Collaboration Initiative

In 2021, the BRCCH and the European & Developing Countries Clinical Trials Partnership (EDCTP) partnered to synergize efforts in mitigating the effects of the COVID-19 pandemic for individuals and society, especially in low-resource settings.

The initiative supports three collaborative projects co-led by BRCCH- and EDCTP-funded researchers across domains related to the impact of COVID-19 on immunology, the need for better diagnostics and novel health screening strategies. Seven lead researchers and 45 collaborators from 14 countries commenced joint research activities and continued this research throughout 2022.

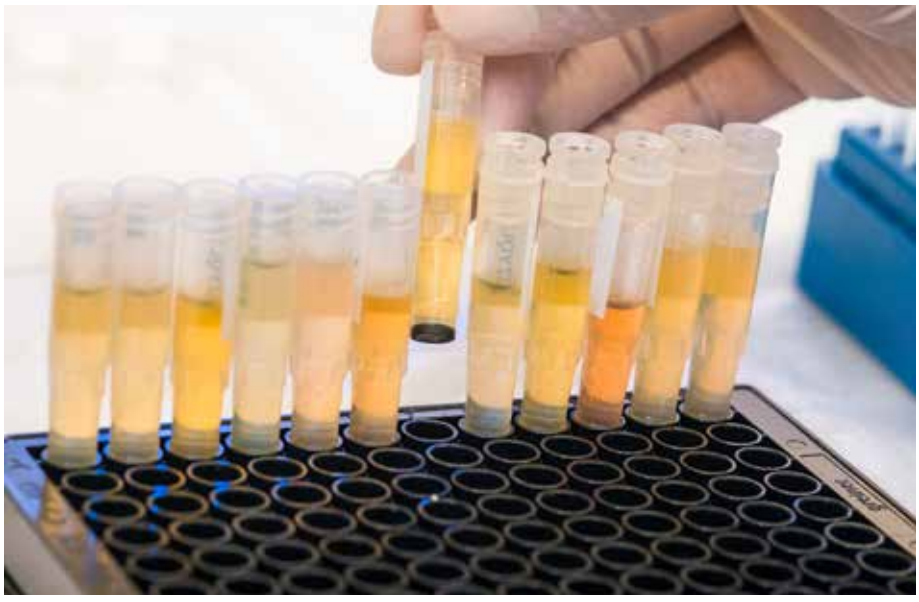
COVID-19 Antibody Repertoires in Infection and Vaccination

Overview: Researchers are studying and comparing the effects of SARS-CoV-2 infection on the memory B cell repertoire at different timepoints and in a variety of patients, such as those who are vaccinated or who contract the virus through natural means. The team aims to longitudinally delineate memory B cell phenotypes and transcriptomes to better understand the generation, function and maintenance of B cells specific to SARS-CoV-2. The project's groundwork in understanding the immune response in COVID-19 will also pave the way for the next waves of the pandemic and for the rapid investigation of other emerging viruses.

Update: The project investigated how natural SARS-CoV-2 infection and/or immunization generates long-lasting protective immunity. The researchers successfully identified SARS-CoV-2-specific B cells in samples of peripheral blood during natural infection or vaccination, and six months and 12 months afterwards, which allowed the team to follow the evolution of SARS-CoV-2- specific B cells from acute to memory phase. Their data showed that SARS-CoV-2 resulted in a resting, stable CD21+ population of memory B cells, which continued to mature for months after infection, and that SARS-CoV-2-specific memory B cells retain a degree of plasticity, enabling the cells to follow different fates and trajectories. They also identified so-called atypical memory B cells, which previous research has detected in the context of chronic infection and autoimmune diseases. In this study, they are now demonstrating that atypical memory B cells can be part of the normal immune response. The formation and role of these atypical cells remain unclear. Overall, the project has contributed a more in-depth understanding of how B cell responses during the acute infection stage correlate to memory formation in the immune response, which may help to inform decisions on prevention strategies during stages of pandemics.

Collaborators: Katie Doores (King's College London, UK); Yakir Guri (University Hospital Basel); Yves Zurbuchen, Onur Boyman (University of Zürich).

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



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 developments in SARS-CoV-2 vaccines, the continuous threat of emerging viral variants means that the most effective control measure remains the detection of infection. 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 solar-powered mobile suitcase lab tailored for point-of-need use in LMICs.

Update: The joint efforts of 11 research groups led to the development of two novel rapid SARS-CoV-2 diagnostics for application in African countries, as well as associated production and assembly lines. In addition, the mobile suitcase lab was customized to enable on-site testing of these diagnostics. The consortium succeeded in completing the analytical validation of the devices and tailoring their design, deployment and use under harsh conditions whilst retaining their key advantages: speed, mobility and price efficiency. The project also significantly supported local capacity-building through the training of young African researchers and the generation of both visual materials for local use and open access online training videos.

Collaborators: Colleagues at ETH Zurich; Leipzig University, Germany; Hemetron AG, Switzerland; Diaxxo AG, Switzerland; Institut Pasteur de Madagascar, Madagascar; Kumasi Centre for Collaborative Research in Tropical Medicine, Ghana; Institut Pasteur, France; Institut Pasteur de Dakar, Senegal; University of Ibadam, Nigeria; Institut National de Recherche Biomédicale, Democratic Republic of the Congo; University of Khartoum, Sudan; Makerere University, Uganda.

Image: A researcher prepares a sample to be analysed in the mobile suitcase lab developed by the collaboration. The portable devices enable researchers to perform the assays at the point of need. Credit: Wisal A. Alrahman and Kamal Eltom.

Lead Researchers

Wendelin Stark
ETH Zurich

Janos Vörös
ETH Zurich

Ahmed Abd El Wahed
Leipzig University, Germany

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: Weak healthcare systems struggle to cope with pandemics. 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. 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 local communities and health authorities and through the deployment of locally developed solutions, the project provides a sustainable and locally grounded COVID-19 response.

Update: In Zambia, the project established a community hub approach with walk-in testing sites to provide screening and testing for COVID-19. In Lesotho, the project deployed a village health worker approach to triage in households or community hubs. Altogether, more than 10,300 people accessed screening services. Qualitative research identified the main barriers to testing; for example, the fear of stigmatization. The main factors that facilitated testing in both Zambia and Lesotho were the ability to travel within and between countries and the need to attend work or school. Ultimately, the project brought together public health stakeholders, researchers and communities for locally adapted solutions and provided important insights for future COVID-19 preparedness and response at the community level.

Collaborators: Lucia Fernandez Gonzalez, Niklaus Labhardt, Tracy Glass, Moniek Bresser, Rahel Erhardt (Swiss TPH); Alain Amstutz, Jennifer Belus (University Hospital Basel); Musonda Simwinga (Zambart, Zambia); Josephine Muhairwe, Bulemba Katende (SolidarMed); Helen Ayles (Zambart, Zambia and 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

Kwame Shanaube
Zambart, Zambia

Postdoctoral Excellence Programme

The BRCCH 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. Its Post-doctoral Excellence Programme (PEP) projects focus on topics from developing tailored medical devices for children and a novel drug strategy to treat an inherited syndrome to harnessing digital solutions to enable personalized medical treatment and care.

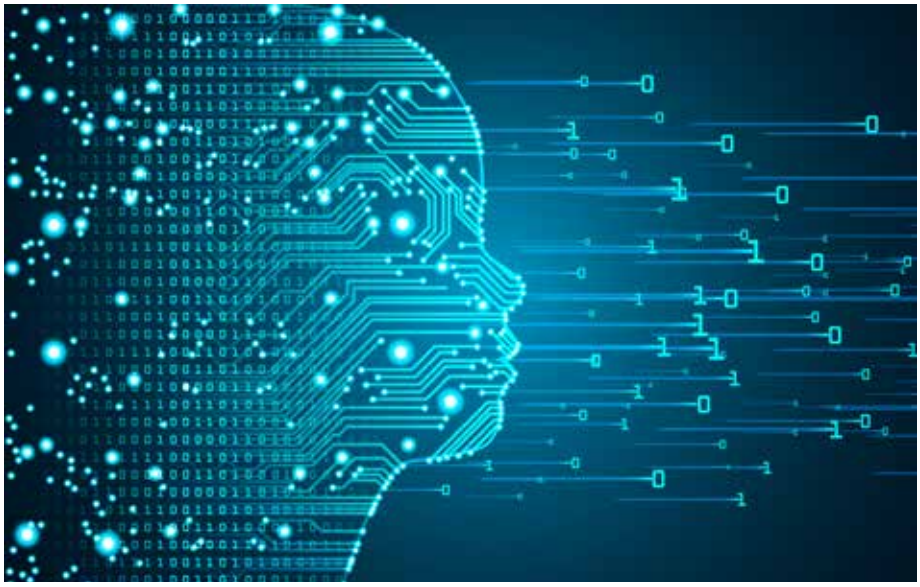
Together with 13 established host principal investigators and collaborators, five highly talented PEP fellows have continued to make progress in their projects, which are three years in duration.

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. There is currently no curative treatment, and owing to the delicate location of these tumours in the brain, treatment options and surgical interventions are limited. Radiotherapy (RT) is one of the few life-prolonging treatments, but its therapeutic efficacy varies between individuals. The current one-size-fits-all therapy is mostly based on clinical experience in adults. In this project, the researchers will bring together tools from separate fields: machine learning and the modelling of tumour growth using differential equations. This combination not only facilitates the identification of which children will benefit from conventional RT, but also informs whether 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 translatable to clinics worldwide that will guide doctors in designing optimal treatment strategies for affected children.

Update: The team identified a patient population at the DMG Centre Zürich and also obtained the first datasets from international collaborators. In parallel, they continued to develop models based on publicly available data, focusing on the prediction of RT response associated with genetic alterations from magnetic resonance images of adult brain tumours, and tested the mathematical modelling pipeline on a different type of paediatric brain tumour. Moreover, the researchers investigated the use of robust training regimes for AI algorithms, the modelling of RT scheduling and the prediction of drug response in paediatric midline glioma through machine learning. Finally, the team's expertise grew with the addition of Prof Catherine Jutzeler, who brings her extensive experience in biomedical data science.

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



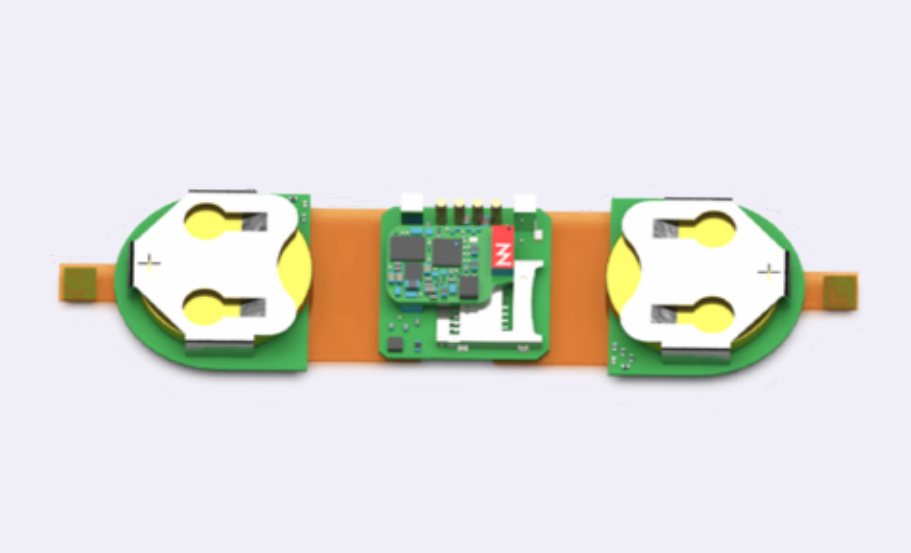
Lead Researchers

Sarah C. Brüningk
ETH Zurich

Catherine Jutzeler
ETH Zurich

Karsten M. Borgwardt
ETH Zurich

Javad Nazarian
University Children's Hospital Zürich



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. 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, non-invasive and autonomous monitoring of multiple vital signs continuously and in real time. The overarching goal is to provide a more effective system for the detection of sepsis via digital biomarkers for better disease management and patient outcomes.

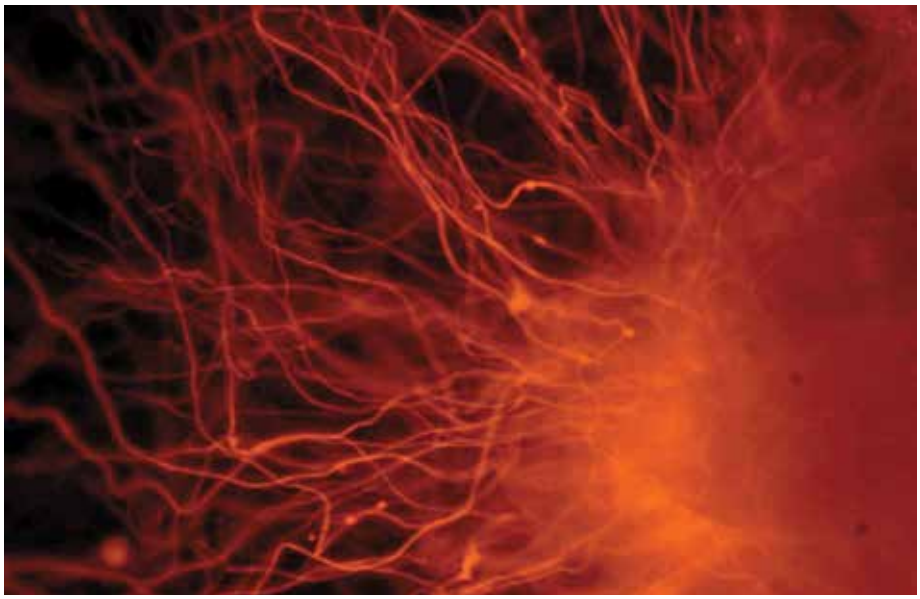
Update: The PATCH-IT project completed a thorough evaluation of current approaches for sepsis identification. From this review, the team determined the most important digital biomarkers to set the range and specifications for the multi-sensor wearable platform. They also designed and developed the first prototype of the PATCH-IT platform to enhance the reliability of the data captured by the wearable sensor and the software that analyses the raw data. This design development was followed by an intense testing phase on healthy adults, which gave further insights into required optimizations. Additionally, the researchers also collaborated with clinicians at University Children's Hospital Zürich regarding the early-stage development of the platform and will continue this partnership during its clinical implementation phase.

Image: Researchers in this project have designed the first prototype of PATCH-IT, a wearable sensor whose aim is to enable the effective detection of sepsis in neonates. 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 are neither very effective nor curative. Existing drugs used for the treatment of this syndrome must be taken throughout life and may pose a financial burden on patients and their families. 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 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.

Update: The researchers succeeded in generating mature organoids from FXS patient-derived stem cells. They found that certain genes implicated in FXS neuronal abnormalities are affected in the early stages of organoid development. They will now use those genes to measure functional recovery or rescue with candidate compounds. In addition, they are currently characterizing the molecular and anatomical profiles of the FXS organoids compared to wild-type controls. Lastly, the project identified a compound that can increase the expression of FMR1 transcription in FXS induced pluripotent stem cells.

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
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 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 healthcare workers for evaluating and managing young patients. However, no such tool has been validated for managing sick infants in outpatient care settings in LMICs. The team will evaluate the effects of an eCDSA for neonates and infants on the quality of care and clinical outcomes in five LMICs. The researchers aim to enhance the prognostic and diagnostic performance of the algorithm using machine learning methods. The project's outputs have the potential to impact millions of sick infants in LMICs and to ultimately reduce mortality in this high-risk population.

Update: In 2022, the team conducted pilot studies at sites in India, Tanzania, Kenya and Senegal, and the resulting findings informed adaptations to the interventions and implementations at study sites. These included changes and updates to the clinical content of the infant algorithms, the features and structure of the eCDSA tool for healthcare workers and the training of healthcare workers to ensure high-quality implementation as well as uptake of the tool for managing sick infants. Training for healthcare workers and data collection began at all sites and intervention implementation also began at three of the sites.

Collaborators: Grace Mhalu, John Maiba (Ifakara Health Institute, Tanzania); Kaspar Wyss, Leah Bohle, Fenella Beynon (Swiss TPH).

Image: Healthcare workers in Senegal pilot test the electronic clinical decision support tool for managing 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

Lead Researchers

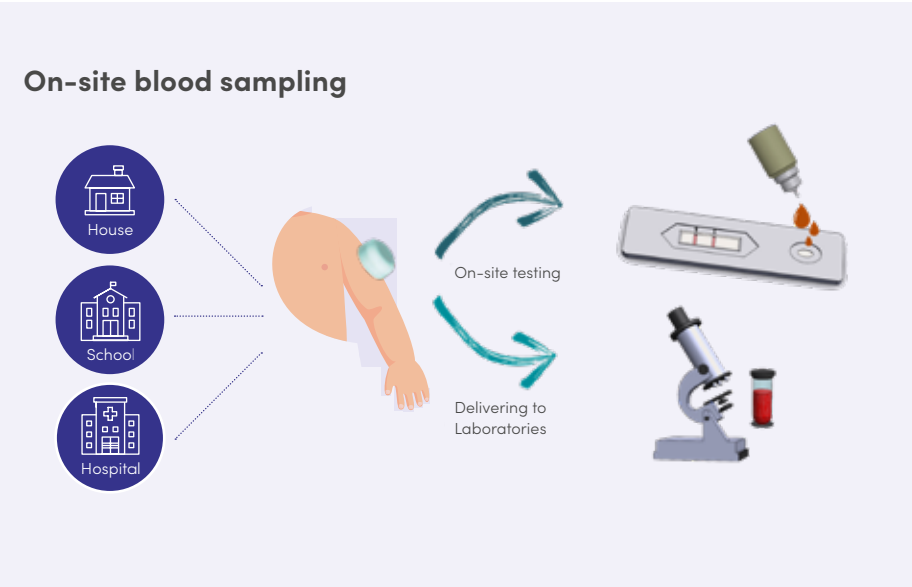
Nicole Zoratto
ETH Zurich

Jean-Christophe Leroux
ETH Zurich

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 blood collection with minimal invasiveness, low manufacturing costs and sufficient volume retrieval for point-of-care tests or laboratory analysis. This device will be specifically designed for children, who are sometimes distressed by traditional blood draws using needles. The researchers will manufacture a prototype via mould-casting and validate it preclinically in combination with a commercially available point-of-care (POC) test for the detection of malaria. In the long term, this device could improve diagnosis and monitoring both in children and in LMICs.

Update: With the aim of making blood sampling both a less traumatic procedure (especially for children) and more accessible in LMICs, the team developed a small patient-friendly and bioinspired device that can extract a small blood volume that is sufficient for rapid testing. Over the past year, they made progress in four key areas: 1) device design for use in resource-limited settings with the identification of the best-performing material; 2) the fabrication process for facilitating its scale-up production; 3) microneedle geometry parameters followed by *ex vivo* testing to enhance their ability to pierce the skin and 4) device assembly including an anticoagulant coating to ensure rapid mixing of blood and anticoagulant.

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.



Principal Investigator Initiative

The Principal Investigator Initiative (PII) aims to drive interdisciplinary research that addresses critical challenges in global paediatric health and medicine. These consortia-based projects bring together researchers from our four partner institutions and international partners who will deliver step-changing innovations and intervention strategies across paediatric health diagnosis, disease treatment and prevention with global reach. The consortia will work to advance the implementation and uptake of strategies in LMICs.

Fifteen lead researchers have teamed up with 38 collaborators across 15 countries in this global endeavour. The six consortia began their activities in autumn 2022 and will continue their projects for four years.

EARLY: Investigating Early Signs and Developmental Course of Personality Disorders in Young People

Overview: Personality disorders (PDs) are frequently occurring mental illnesses that have devastating effects on both afflicted individuals and society. Until recently, these disorders were primarily diagnosed in adulthood, although it is now well established that their first signs are detected already during childhood and adolescence. Since its implementation in January 2022, the 11th edition of the World Heath Organization's International Classification of Diseases (ICD-11) has been facilitating a radical shift in the diagnostic classification of PDs. This shift abandons the categorical system in favour of an assessment of dimensional personality functioning and eliminates the age restriction for evaluation. This project aims to investigate whether this new concept is valid and useful for diagnosing and assessing personality impairments in children and adolescents, as it is in adults. Through multi-site longitudinal studies, the consortium will develop approaches to investigating the early signs and progression of PDs in a comparable way across different cultures, age groups and socio-economic settings.

Collaborators: Hojka Gregoric Kumperscak (University Medical Center Maribor, Slovenia); Sylvia Kaaya (Muhimbili University of Health and Allied Sciences, Tanzania); Delia Birle (University of Oradea, Romania); Rasa Barkauskiene (Vilnius University, Lithuania); Moises Kassin (Universidad Iberoamericana Ciudad de México, Mexico); Eva Möhler (Saarland University Hospital, Germany); Carla Sharp (University of Houston, USA); Diane Purper-Ouakil (University of Montpellier, France); Natalia Zvereva (Moscow State University, Russia); Kathrin Sevecke (Innsbruck University Clinic for Psychiatry, Austria); Lea Sarrar (MSB Medical School Berlin, Germany); Sefa Cosgun (Private Clinic, Istanbul, Turkey); Felix Euler (Juvenile Forensic Department, Zürich, Switzerland); Michael Kaess (University of Bern, Switzerland).

Image: The personality is shaped during childhood and adolescence. Researchers aim to develop approaches for the early diagnosis of personality disorders using a new concept of personality functioning domains and thus lay the groundwork for more timely intervention. Credit: Marc Birkhölzer.

Lead Researchers

Marc Birkhölzer
University of Basel

Alex: Design, Development and Evaluation of a Digital Health Assistant for Paediatric Asthma

Overview: Poor adherence to medication and insufficient monitoring are key factors that contribute to inadequate asthma control in children and adolescents. This project aims to improve asthma control in adolescents using a smartphone-based digital health assistant (DHA) called Alex, which is designed for remote disease monitoring and patient coaching. This novel, age-specific longitudinal telemonitoring system will track lung function and inflammation (measured by the patients using portable paired biomedical devices), environmental exposures and medication adherence in young asthma patients. Furthermore, it will motivate the patients and keep them engaged and committed to the disease monitoring schedule by implementing various incentives and strategies known in the field of behavioural economics, including gamification approaches. Moreover, through digital and AI-based approaches to passively assess the patient's health status, this technology's goal is to minimise the burden of self-monitoring for young patients. In addition, the data collected will be used to train machine learning models to be used for disease progression prediction and as clinical decision support algorithms.

Collaborators: Urs Frey (University Children's Hospital Basel); Filipe Barata (ETH Zurich); Nicole Probst-Hensch (Swiss TPH); Sorin Man (Emergency Clinical Hospital for Children, Romania); Ioana Ciuca (Victor Babeş University of Medicine, Romania); Roxana Maria Nemes (Titu Maiorescu University, Romania).

Image: A patient holds a portable lung inflammation assessment device that communicates with the digital health assistant, Alex, on their smartphone. The researchers envision Alex as a playful and effective way for patients with asthma to always carry their "doctor" in their pocket, thereby empowering individuals to actively participate in the management of their condition. Credit: Center for Digital Health Interventions at ETH Zurich and Bosch Healthcare Solutions GmbH.

Lead Researchers

Edgar Delgado-Eckert
University Children's Hospital Basel and University of Basel

Elgar Fleisch
ETH Zurich

Torsten Schmitz Cherdron
Swiss TPH

FACEIT: Feasibility and Economic Evaluation of Improved Child Deworming

Overview: Parasitic worm infections are still very common, particularly among children living in areas with limited access to safe drinking water and adequate sanitation. Additionally, these children are at the highest risk of morbidity associated with chronic worm infections. Current disease control efforts consist of the mass distribution of medications to schoolchildren without prior diagnosis. These interventions often do not cure a large proportion of the treated children, since these drugs show low cure rates against some parasitic worm species or are not suitable for administration to young children. This project aims to evaluate the introduction of a promising and safe combination therapy to use against soil-transmitted helminth infections in routine disease control activities in Uganda. Moreover, the consortium will assess the feasibility, acceptability and cost-effectiveness of new child-deworming treatments and develop delivery toolkits that are effective in local settings. Overall, the project aims to contribute to the advancement of worm infection management affecting young children in LMICs and to support policy change at national and international levels.

Image: A healthcare worker oversees a child taking a pill during mass drug administration activities in a Ugandan school. Credit: Moses Adriko.

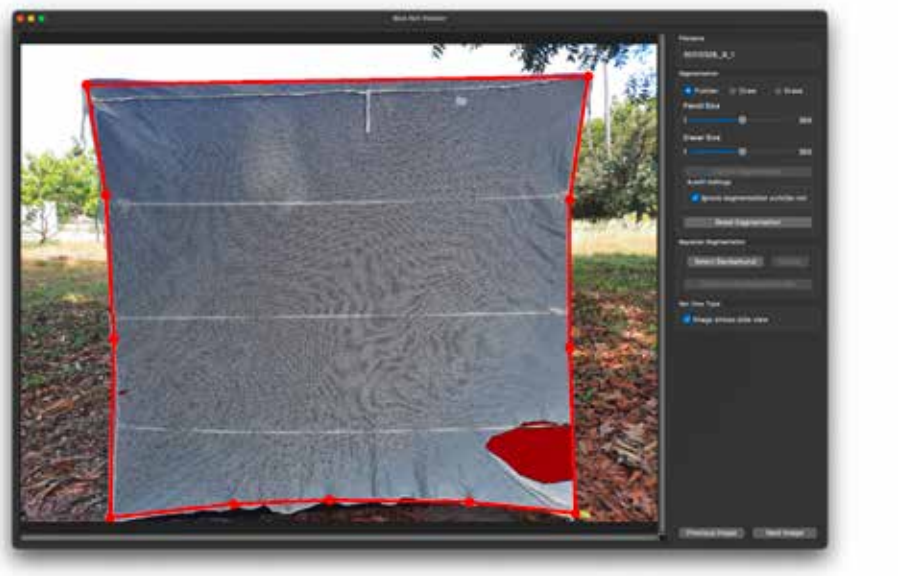
Lead Researchers

Jennifer Keiser
Swiss TPH

Fabrizio Tediosi
Swiss TPH

Peter Steinmann
Swiss TPH

Moses Adriko
Ministry of Health, Uganda



ViALLIN: Visual Analysis of Long-Lasting Insecticidal Nets to Maximise Universal Access

Overview: Children under the age of five living in sub-Saharan Africa are the age group most affected by malaria. Long-lasting insecticidal nets (LLINs, referred to as bed nets) have been vital in reducing the malaria burden among children. However, more than 50% of people living in endemic areas are currently unprotected because LLINs often develop holes sooner than expected, leaving millions of children unprotected. The goal of this project is to develop a digital tool, ViALLIN, that will allow researchers to collect images of LLINs and to measure their durability based on surface hole area analysis. The data will enable national malaria control programmes to improve planning for programmatic LLIN distribution, monitoring of LLIN quality and selection of the best product for use according to contextual settings. By providing information on mosquito net lifespan, the project aims to optimize resource use, increase the protection of children and reduce malaria transmission in LMICs.

Collaborators: Noela Kisoka, Fabrizio Tediosi, Gianpaolo Pontiggia, Sumaiyya Thawer (Swiss TPH); Julia Wolleb, Natalia Manas Chavernas, Robin Sandkühler (University of Basel); Emmanuel Mbuba, Zawadi Mboma (Ifakara Health Institute, Tanzania); Frank Chacky, Allan Kimweri, Charles Dismas Mwalimu (Ministry of Health, Tanzania).

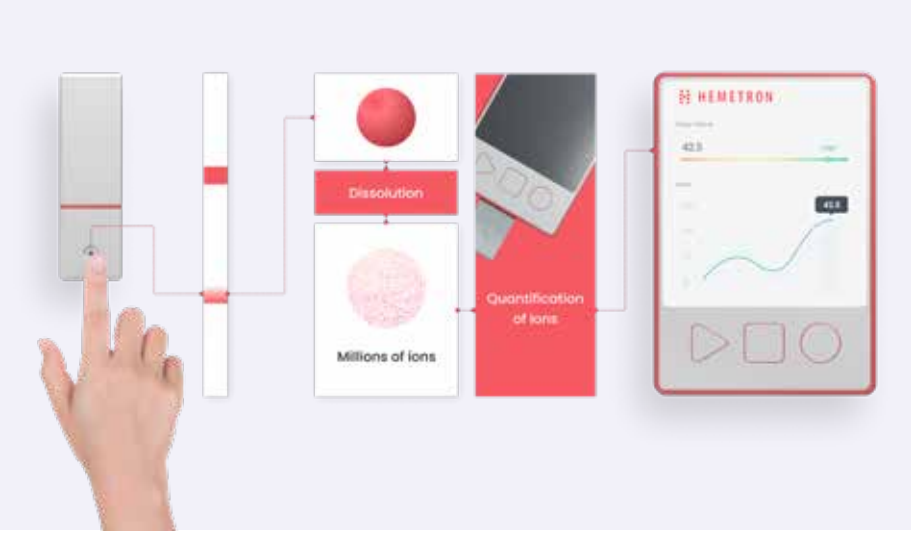
Image: The digital tool ViALLIN will use surface hole analysis to assess the quality of long-lasting insecticidal nets. Credit: ViALLIN consortium.

Lead Researchers

Sarah Moore
Swiss TPH

Philippe Claude Cattin
University of Basel

Amanda Ross
Swiss TPH



TOOLS4BU: New Tools for Early Diagnosis and Decentralized Treatment of Buruli Ulcer

Overview: "Buruli ulcer" is a chronic necrotizing skin disease caused by *Mycobacterium ulcerans*. This bacterium triggers skin ulcers that continuously expand over extended periods if they are not treated appropriately. This debilitating disease primarily affects children living in West and Central Africa and most infections occur in remote regions where patients have limited access to appropriate medical care. This project aims to develop a simple point-of-care diagnostic test and an efficient treatment for Buruli ulcer that can be easily implemented at the primary healthcare and community levels in rural areas. Ultimately, the consortium seeks to prevent long-term suffering, stigmatization and permanent disabilities in afflicted children who live in Buruli ulcer-endemic countries in Africa.

Collaborators: Gerd Pluschke (Swiss TPH); Alexander Tanno (ETH Zurich and Hemetron AG).

Image: Researchers will develop a rapid diagnostic device to detect Buruli ulcer, a chronic necrotizing skin disease. Credit: Hemetron AG.

Lead Researchers

Daniel Paris
Swiss TPH

Janos Vörös
ETH Zurich

OptiThyDose: Intelligent Digital Decision Support Tool to Personalise Dosing for Children with Thyroid Diseases

Overview: Hypo-/hyperthyroidism manifests at birth or during childhood. Prompt and adequate medical treatment is key to protecting normal cognitive and physiological development in affected children. Dose optimization is complex given the wide spectrum of thyroid disease severity and activity, age-specific pharmaco-dynamics and inter-individual variability in drug kinetics and thus clinical response in these children. Hence, there is frequent over- or under-dosing despite international treatment guidelines. This project aims to develop an intelligent decision support tool, OptiThyDose, that computes and optimizes personalized dosing for children afflicted with a thyroid disease. OptiThyDose iteratively computes individual dose regimens based on the patient's age, weight and disease severity to restore and maintain correct thyroid hormone concentrations. The researchers will conduct an international multi-centre study to validate and facilitate the clinical use of OptiThyDose in different socio-economic settings.

Collaborators: Michel Polak (Hôpital Necker-Enfants Malades, France); Marco Cappa (Ospedale Pediatrico Bambino Gesù, Italy); Lusine Navasardyan (Arabkir Medical Centre, Armenia); Johannes Schropp (University of Konstanz, Germany).

Image: A clinician and a child use a model of the thyroid to talk about the hormones it produces and their importance for brain development, growth and puberty. Credit: Pixel-Shot.

Lead Researchers

Gabor Szinnai
University Children's Hospital Basel

Marc Pfister
University Children's Hospital Basel

Together with international collaborators, BRCCH researchers aimed to improve the diagnosis and triage of COVID-19 cases at the hospital level and fortify access to essential health services in resource-constrained settings. The MistraL team in Lesotho provided screening for nearly 180,000 adults and children for COVID-19/tuberculosis symptoms or recent exposure to COVID-19. A related BRCCH- and EDCTP-funded project in Lesotho and Zambia demonstrated the feasibility of testing by lay health workers using different strategies to identify COVID-19 cases in the community, as well as self-testing for SARS-CoV-2. Credit: MistraL and BRCCH.

Outputs and Communications

BRCCH-funded researchers make it a priority to publish, share and apply their research findings. The Centre commends their additional dedication to open access research, science communication and capacity-building efforts.

45 papers in peer-reviewed journals, with 93% of them open access

4 steps towards technology transfer via patent applications

92 research presentations (talks, seminars and posters)

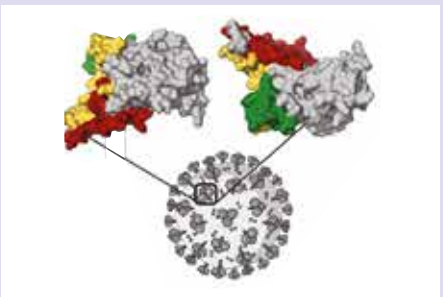
58 capacity-building efforts (educational lectures, conference organization, outreach activities, training sessions, theses)

35 research disseminations in the news and media

Lessons from the Deceased to the Living and Back

Manina Etter, together with Prof Gregor Hutter, Dr Matthias Matter, Prof Alexandar Tzankov and colleagues, published their seminal work on Neuro-COVID in the journal *Nature Communications.* This study involving COVID-19 patients with different degrees of neurological symptoms revealed that Neuro-COVID can cause alterations in the brain's structure. The team also found that patients with severe Neuro-COVID harbour molecular alterations in their blood and cerebrospinal fluid that are associated with abnormal immune responses. They now aim to investigate the use of these molecular signatures as predictive biomarkers for severe Neuro-COVID in the future. Credit: Caroline Eich.

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



The consortium led by Prof Sai Reddy developed an artificial intelligence method, deep mutational learning, which predicts the ability of SARS-CoV-2 variants to bind to human cells and escape antibodies. This information may guide the future development of therapeutic antibody treatments and next-

generation vaccines. Predictions can also be generated in real-time to aid faster public health decision-making. This significant work was published in the journal *Cell* and has led to new collaborations with industry and other international research groups to screen next-generation antibodies for escape by virus variants and potentially guide the selection of future antibody therapeutics. The resulting collaborative work was published in multiple papers in the journal *Lancet* and attracted coverage from the *New York Times* newspaper. Credit: Taft et al. 2022.

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

BRCCH Postdoctoral fellow Dr Kanika Dheman, together with Prof Michele Magno, has prototyped an innovative wearable sensor for neonatal monitoring. To facilitate capacity-building efforts, they and fellow members of the Center for Project-Based Learning taught a hands-on course to ETH Zurich bachelors students in order to introduce them to the design and development of wearable electronic devices. The students applied the principles of electronic design, firmware development, data quality and product usability. Additionally, their research received the best paper award at the tenth International Workshop on e-Health Pervasive Wireless Applications and Services 2022. Credit: K. Dheman and M. Magno, Center for Project-Based Learning.

Living Microbial Diagnostics to Enable Individualized Child Health Interventions

The consortium led by Prof Randall Platt published ground-breaking research using CRISPR engineering to develop a non-invasive, microbe-based diagnostic for measuring gut health in the prestigious journal *Science.* In addition to this publication, the consortium members received multiple awards. Prof Platt was named a winner of the Falling Walls Foundation Life Sciences award, which highlights renowned researchers who are making significant scientific breakthroughs towards addressing the world's biggest challenges. Postdoctoral researcher Dr Florian Schmidt received the ETH medal and the 2022 Rainer Rudolph Prize for his excellent doctoral thesis on advancing this technology, and he was also awarded the 2022 Science & SciLifeLab Prize for Young Scientists. Credit: Troyan.

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

This BRCCH-EDCTP collaborative project involving 11 research groups across Switzerland and Africa propelled the development and clinical validation of two novel rapid SARS-CoV-2 diagnostic devices to meet three key needs in LMICs: speed, mobility and price efficiency. Over 1,500 diagnostic devices were produced and deployed for testing by trained local collaborators across nine African countries. In addition, BRCCH researchers Prof Wendelin Stark and Dr Michele Gregorini successfully obtained CE marking for their novel peakPCR device, a pivotal step towards making this device globally available to those most in need. Credit: Soa Fy Andriamandimby.

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

The project successfully supported the screening and triaging of patients for COVID-19 and tuberculosis in northern Lesotho. The researchers validated rapid diagnostics for COVID-19 and deployed an artificial intelligence software tool (CAD4COVID) for radiographs in combination with white blood cell count. They shared their achievements and preliminary results at stakeholder meetings with district and local medical officers and management members, community health workers and healthcare partners. The participants shared their own experiences of performing similar implementation activities and discussed how to facilitate local access to results. The project results were also shared with the COVID-19 research community and the government of Lesotho. Credit: MistraL.

Meet the Advisory Board

The members of the BRCCH's Strategic Scientific Advisory Board (SSAB) apply their expertise and experience in order to guide the Centre on how best to achieve its vision. Together, its seven members possess considerable complementary knowledge and know-how relevant to the BRCCH's scope and mission. We are grateful for their commitment to the Centre and their expert guidance.

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 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 the United Nations Children's Fund (UNICEF) 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 Margaret Gyapong 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.

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 in 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.

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.

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

Interview & Insight

Prof Marcel Tanner sat down with the BRCCH to talk about how the momentum and successes of the Centre's first years are shaping its future. He also shared his insight into how joy can help us to contribute to improving young people's health.

BRCCH: Prof Tanner, in addition to being part of the Fondation Botnar Board, you have also been an integral member of the BRCCH's SSAB since the Centre's very beginning. You therefore have a unique perspective and insight into the BRCCH. Could you tell us about how you witnessed the Centre's inception?

Prof Marcel Tanner (MT): I joined the Fondation Botnar Board in 2018. Already at that time, there was a plan to establish a research centre focused on paediatric health, and we had always intended to do this in partnership with the University of Basel and ETH Zurich. Fondation Botnar considers child and adolescent health, well-being and nutrition, as well as protection and education, to be very important for the future of the world's young generation. This philosophy shaped the goal that the BRCCH should become a major crystallization point for innovation where one can actually advance child and adolescent health and well-being.

There were two important principles that guided the working process. The first was that different disciplines should be brought together so that solutions would be transdisciplinary and applicable. The second was that these solutions must be developed along the value chain, from innovation to validation to application in real-world settings. If one can develop and validate innovations that are generalizable for the population(s) of concern, then one can bring them to the people who need them most. This is why the BRCCH focuses on developing solutions that can reach children and young people living in low- and middle-income countries. These two principles require that this be pursued in partnership, as no single institution can achieve this feat alone. We therefore involved all of the parties when planning the set-up of the BRCCH. We must come together in order to make paediatric solutions work, and this is what gathered and motivated us to form the BRCCH.

BRCCH: We are now in our fourth year of operations. What is your view of the Centre's activities over the past years?

MT: It has had a very good start. I would first like to congratulate the leadership of the BRCCH for really pursuing the two guiding principles behind the Centre's founding. These ideas are not necessarily easy to implement in a dynamic landscape that involves many stakeholders. The BRCCH has made substantial progress. It is important that we reflect on where the Centre is now in order to keep up the momentum and to successfully move forward to where it wants to and can be.

BRCCH: What are some of the challenges that the BRCCH faces and how does the SSAB assist it in meeting them?

MT: This question relates to the second principle that solutions must be applied along the value chain so that they can be implemented in real-world settings. That can be a challenge. This is where we as SSAB members contribute our advice based on our expertise and experience. Sometimes, it is not easy to make strategic investments in research to really advance the field of child health in a dynamic scientific landscape. On the one hand, we have the global problems in child and adolescent health, education, protection and well-being. On the other, there are constraints in the landscape that are not conducive to translating a research project into generalizable health solutions. There are no "one-size-fits-all" solutions: for those most in need, solutions must be

"Joy is an important component of creating the right atmosphere for change: the joy of being curious to discover solutions, the joy of sharing and having a process of mutual learning and the joy of seeing things translated into action."

Prof Marcel Tanner

tailored to a given health and social system in order to have an impact.

The BRCCH's research portfolio includes projects that are good examples of the principles of translatability and transdisciplinarity. In general, we must create the right atmosphere to successfully carry out these principles. The important question for the BRCCH now is how we can keep the momentum going and surpass what is considered standard.

BRCCH: Thank you, Prof Tanner, for your time. Before we finish, do you have any last thoughts to share?

MT: Thank you. This is an exciting time. There is a lot on the horizon and we should continue to follow the BRCCH's vision to improve child and adolescent health. We need to ensure good outcomes from the Centre's research efforts, and then global impact will follow.

I would like to end by saying that in an initiative like the BRCCH, one should have joy related to three things. This idea has carried me through life. First is the joy of discovery; i.e., doing research. If one is curious like a child, instead of only seeing difficulties in the world, one asks questions. Questions demand answers, and that means discovering solutions that can be applied to a biological system or all the way up to a societal system. This also provides the basis for excellence in science. The second is the joy of sharing. We can teach one another and learn more not only through collaboration, but through a partnership based on a process of mutual learning for change – that really moves us forward. The third is the joy of seeing things being translated into action. We need to be a part of this translation to ensure that the research reaches the main beneficiaries: young people in resource-limited settings.

Pursuing these three joys will allow us to reach a critical point where we also see the outcomes of the BRCCH's efforts and will enable us to make a small contribution to a better world. That is the overall spirit that the BRCCH should maintain.

"We must come together in partnership to really make paediatric solutions work."

Prof Marcel Tanner

Governance and Finances

Governance
The BRCCH Board comprises representatives from the University of Basel and ETH Zurich, and together they oversee the BRCCH's strategy and activities. Director Prof Georg Holländer and Vice Director Prof Sai Reddy are the Centre's academic leads and are thus responsible for implementing the BRCCH's strategy and directing its operations. The Strategic Scientific Advisory Board (SSAB), comprising national and international experts, advises the Directors and the Board based on their extensive expertise in domains relevant to the BRCCH's remit. An ad hoc Project Evaluation Board (PEB) is responsible for the independent scientific review of projects submitted to individual funding calls.

Finance
The BRCCH benefits from a generous donation of a total of CHF 115 Mio from Fondation Botnar to support its activities up to 2028. This budget 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. Grants in the BRCCH funding programmes are available to clinical and research investigators from our four partner institutions and their national and international collaborators. While continuing to run the established funding programmes, the BRCCH is looking forward to including support for professorships in its current portfolio.

Thanks
The BRCCH would like to sincerely thank Fondation Botnar for their generous support and the fruitful interactions had in the past year. The Centre also wishes to thank all board members for their active contributions to the BRCCH in the course of the the past year. We extend a special thanks to Prof Detlef Günther, whose involvement on the BRCCH Board and tenure as Vice President for Research and Corporate Relations at ETH Zurich ended at the close of 2022. It has been a pleasure and a privilege to work with Prof Günther.

BRCCH Board

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

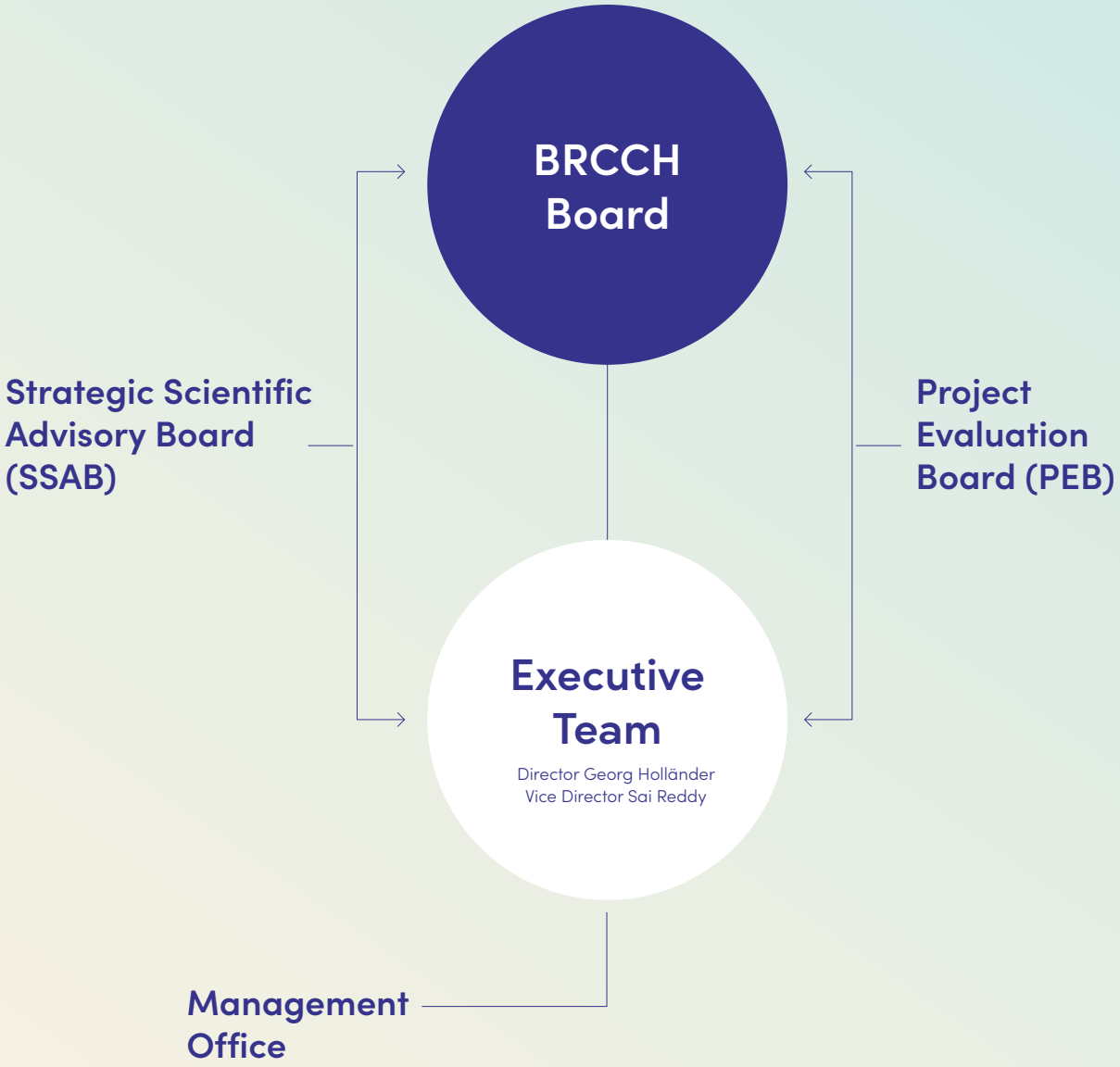
Prof Detlef Günther
Co-Chair of BRCCH Board and
Vice President for Research and
Corporate Relations at ETH Zurich

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 Laura Nyström
Head of the Department of
Health Sciences and Technology
(D-HEST) at ETH Zurich


BRCCH Board
Strategic Scientific Advisory Board (SSAB)
Project Evaluation Board (PEB)
Executive Team
Director Georg Holländer
Vice Director Sai Reddy
Management Office

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Impressum
Publisher: Botnar Research Centre for Child Health
Editors: Maressa Takahashi
Proofing: Katharine Handel
Design: STUDIO NEO, Basel
Print: Birkhäuser+GBC AG, Basel
Print run: 200 copies

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