BRC CH Basel Research Centre for Child Health

Annual Report 2025

Basel Research Centre for Child Health

University of Basel ETH zürich

Supported by Fondation Botnar

Dear BRCCH community,

Prof Georg Holländer
BRCCH Director

Prof Daniel Müller
BRCCH Co-Director

With 2025 now behind us, we reflect on an intense and eventful year. Last year, the BRCCH advanced its strategic transition from a project-funding agency to a paediatric digital health hub. Two new BRCCH professors were appointed at the University of Basel: Dr Ece Özkan Elsen, Professor in Paediatric Digital Health Data as of February 2025, and Prof Dr Burcu Tepekule, Professor in Paediatric Infectious and Non-Infectious Emerging Diseases Modelling as of August 2026. Together with Prof Na Cai at ETH Zurich and three soon-to-be-appointed professors, they will develop novel digital and data-driven research methods. By addressing the preventive, diagnostic and therapeutic challenges faced by paediatric patients worldwide, they will ensure that the BRCCH continues to be an impact-driven organization.

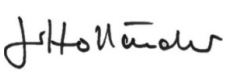
The past year has also seen the start of the work on the new BRCCH building, which will host the six BRCCH professors, their associated research teams and the executive office. By bringing together academic leadership, research activity and strategic management under one roof, the new facility will foster interdisciplinary exchange, operational efficiency and innovation, thereby supporting the BRCCH's long-term strategic objectives.

In parallel with the establishment of the new centre, the BRCCH carried on with its research funding activities. The research consortia from the Multi-Investigator Programme continued harvesting the fruits of their research efforts, developing cellular-based methods for personalized diagnosis as well as digital medical interventions.

Similarly, researchers from the Principal Investigator Initiative continued their projects, whose outcomes and impact were examined by a panel of external experts in a mid-term evaluation. Moreover, the Centre launched a new internship programme in paediatric digital health designed to support capacity building and knowledge transfer from BRCCH researchers and scientists from the Global South; although it is still in its pilot phase, the programme has already supported four researchers by providing access to the expertise and research environment of BRCCH-associated institutions.

In this Annual Report, we are pleased to present a summary of the BRCCH's activities over 2025. This work would not have been possible without the generosity of our funder, Fondation Botnar, and the support of our partner institutions, the University of Basel, ETH Zurich, University Children's Hospital Basel (UKBB) and the Swiss Tropical and Public Health Institute (Swiss TPH).

With our best wishes,



Prof Georg Holländer

Prof Daniel Müller


Messe
Johanniterbrücke
Zentrum Nord
St. Johann
Kinderspital (BRCH)
Universitätsspital
Storchen
St. Peterer

A Paediatric Digital Health Hub

In 2024, the BRCCH started to transition towards becoming a paediatric digital health hub embedded within the University of Basel and ETH Zurich. In its new form, the Centre is bringing together six new professorships – three affiliated with the University of Basel and three affiliated with ETH Zurich – working collaboratively within a new research facility located at the Life Science Campus in Basel. The research activities of these professorships will be dedicated to a wide range of topics, spanning from new cellular-based tools for precision diagnostics to innovative computational methods for analysing big health datasets. Complementary to these research activities, two capacity-building platforms will strengthen the research efforts of the Centre as a whole.

Significant progress was made in the recruitment of BRCCH professors over the last year. At ETH Zurich, the Professor in Medical Genomics, Prof Na Cai, started her research activities in February 2025. Moreover, the professorship in Clinical Evaluation of Paediatric Digital Health will be re-advertised in 2026 and an appointment regarding the professorship in Biomolecular Engineering for Health is expected over the course of 2026.

At the University of Basel, Prof Ece Özkan Elsen started her research activities in February 2025. On 28 November, Dr Burcu Tepekule was appointed to the professorship in Paediatric Emerging Infectious and Non-Infectious Diseases Modelling. She will start her new position in August 2026 by seeking to characterize the interplay between the immune system and the gut microbiota during the first years of life. Finally, six talented candidates for the professorship in Systems Developmental Medicine were invited to deliver talks and conduct in-depth interviews about their current and future research projects in December 2025. An official appointment is expected in the course of 2026.

Image on page 4: 3D reconstruction of the future BRCCH building at the corner of Schanzenstrasse and Spitalstrasse. Credit: Guerra Clauss Garin Architects.

Another important milestone towards the establishment of the new paediatric digital health hub occurred in September 2025, when the work on the new BRCCH building began with the demolition of the current building. Expected to be fully operational by the end of 2027, the new building will provide a dedicated space for the six new professors and their research groups, significantly strengthening the institution's research capacity while accelerating scientific innovation.

Further descriptions of the research activities of the BRCCH professors, alongside those of the BRCCH-affiliated Prof Daniel Baumhöer, are presented in the following sections.

Image: A virtual reconstruction of the new building, where all BRCCH professors and the executive team will be allocated. Credit: Guerra Clauss Garin Architects.

Genetics of depression: from statistical associations to molecular understanding

Lead Researcher

Prof Na Cai
ETH Zurich

Major Depressive Disorder (MDD) is a debilitating mental condition that manifests with a wide range of clinical symptoms, including depressed mood, anhedonia or sleep disturbance. A significant proportion of depression cases begin in childhood and increase dramatically during adolescence, with a MDD lifetime prevalence of 11 to 19% in 13- to 18-year-old adolescents. Depressive episodes in adolescence often predict emotional challenges, academic difficulties and a higher risk of self-harm and suicide in adulthood. Yet the early identification of people at risk of developing MDD remains challenging to date.

This is largely due to the polygenic and heterogenic nature of this mental disorder. Unlike many other diseases, in which a malfunction of one or a few genes can explain disease pathology, thousands of genes contribute to MDD in different etiologically relevant combinations. This heterogeneity is partly reflected in the marked differences in symptoms, disease course and treatment response among individuals sharing the same MDD diagnosis.

To improve the diagnosis and treatment of MDD, Prof Cai seeks to develop and implement quantitative genetic and statistical methods to understand the molecular basis of MDD subtypes. The first step towards this goal is the identification of genetic variations underlying MDD and its symptoms using genome-wide association studies (GWAS). These population-based approaches identify common genetic patterns in individuals with the same clinical phenotype. In order to obtain clinically relevant data, the study will need to analyse big datasets from patients clinically diagnosed with MDD.

As detailed clinical assessments of MDD are rarely available in the large numbers necessary for such analysis, Prof Cai's group works on mining and deriving clinically relevant data from biobanks and Electronic Health Records (EHRs), using both statistical and deep-learning methods to extract useful information from incomplete or biased data. In particular, the group is working on methods that integrate disease-relevant measures (e.g., clinically administered questionnaires, laboratory parameters, imaging, biomarkers) with raw EHRs diagnostic data to generate valid inferences regarding lifetime susceptibilities to diseases for each individual in an EHR.

A further goal of Prof Cai's research is to understand the biology behind MDD, including how our genes, brain, body and life experiences - such as stress - interact to influence mental health. To this end, her group is developing and implementing computational models to predict the multi-omic (i.e., transcriptional, genomic and metabolic) profile of patients with MDD. Profile comparisons of control vs depressed individuals will enable the identification of not only the genes responsible for different subtypes of MDD, but also the cell types and signalling pathways in which they are involved. Complementary to this approach, Prof Cai's group has also developed Bayesian methods to identify genes with aggregated rare variants effects, which will help her to identify the most disease-relevant genes causing MDD. Finally, she is using single-cell gene expression data from mice exposed to chronic stress to explore how stress, a major risk factor for MDD, may change the expression levels of some neuronal genes involved in this mental disorder.

Overall, Prof Cai's research will contribute to identifying individuals at risk of developing MDD, minimizing misdiagnosis, guiding preventive strategies and ultimately improving the outcomes for individuals living with depression.

Lead Researcher

Prof Na Cai
ETH Zurich

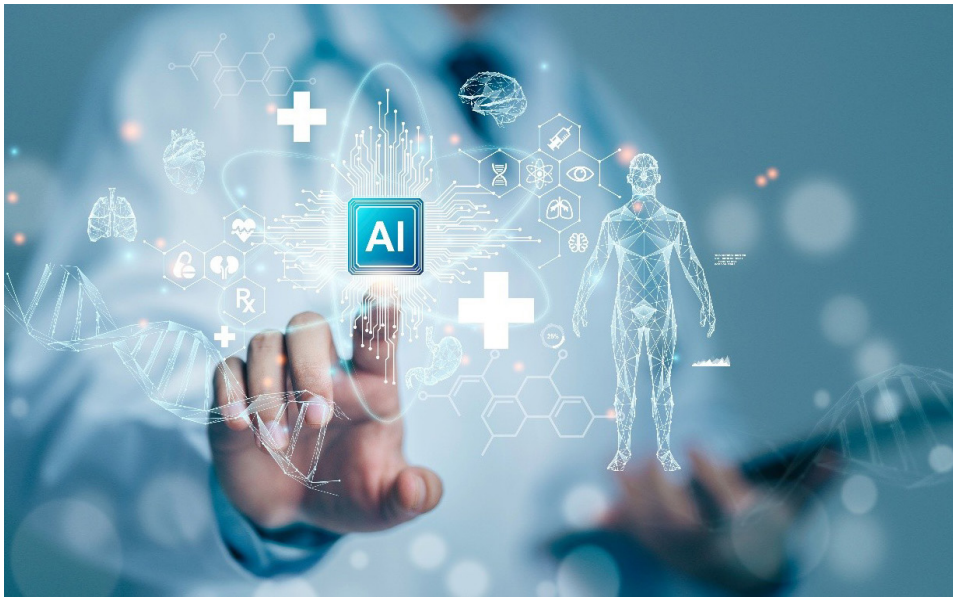
Multimodal Health – Generalizable Artificial Intelligence Models for Paediatric Clinical Applications

Lead Researcher

Prof Ece Özkan
University of Basel

Artificial Intelligence (AI) and its ability to derive medical predictions based on patterns from existing clinical datasets has attracted substantial attention in clinical medicine over the last years; it has the potential not only to support precision diagnosis, but also to personalize treatment options and risk stratification. In particular, data-driven models applied to medical images, physiological signals (e.g., heart rate, brain activity) and structured clinical data offer new opportunities to improve clinical decision-making. However, the integration of machine-learning models into real-world clinical practice remains challenging, especially in complex, data-scarce settings such as paediatrics.

Many AI-powered models, unlike physicians, are unable to integrate multiple types of data. They are developed for single data modalities, focus on organ- or disease-specific tasks and often fail to generalize across hospitals, populations and age groups. Moreover, models trained in one clinical context frequently show lower performance when transferred to new patient cohorts or hospitals. Addressing these limitations requires methods that can integrate heterogeneous data sources while remaining robust, interpretable and transferable.



Prof Özkan Elsen's research addresses these challenges by developing multimodal and longitudinal AI models that jointly learn from medical imaging, physiological time series and structured clinical data. Drawing inspiration from human clinical reasoning, her work focuses on data fusion architectures that enable models to combine complementary information across modalities and time, thereby improving generalization and clinical relevance.

A central focus of Prof Özkan Elsen's research is the development of trustworthy AI for paediatric medicine. Many AI models are primarily trained on adult cohorts and fail to account for fundamental physiological and clinical differences between adults and children, such as ongoing organ development and age-dependent disease patterns. To address this gap, she develops uncertainty- and bias-aware modelling approaches that explicitly quantify model confidence and ensure reliable performance across age groups.

By advancing methods for generalization, interpretability and rigorous uncertainty quantification, Prof Özkan Elsen's research aims to enable AI systems that clinicians can safely trust in paediatric settings. In the long term, these efforts will contribute to more equitable and reliable clinical decision support tools, helping to overcome long-standing challenges in paediatric care where limited data availability has historically constrained early diagnosis and personalized treatment for children and adolescents.

Lead Researcher

Prof Ece Özkan
University of Basel

The Power of Epigenetics – Advancing the Diagnosis of Bone and Soft Tissue Tumours

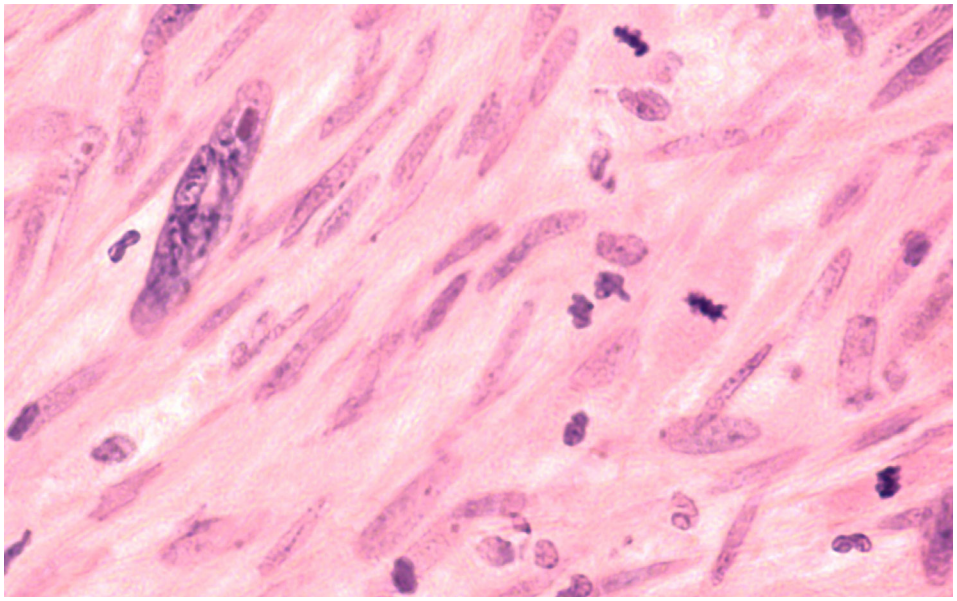
Lead Researcher

Prof Daniel Baumhoer
University of Basel

Bone and soft tissue tumours are rare, but they represent the most common type of tumours in children and adolescents after leukaemia, lymphoma and brain tumours. They encompass over 175 subtypes of tumours and their clinical presentation is often non-specific, with painless or slowly growing masses that can be mistaken for benign conditions. In addition, they lack specific molecular markers, further complicating their classification and, in turn, diagnosis. Yet a timely and accurate diagnosis remains crucial for guiding appropriate treatment and improving health outcomes in affected children.

Traditionally, tumour diagnosis has relied on imaging studies and the histological examination of biopsy samples. However, methylation profiling has recently begun to emerge as a promising diagnostic approach to classifying neoplasms. By analysing characteristic patterns of methylation throughout the genome, this innovative method contributes to a more unambiguous classification of tumours, as most tumour types exhibit distinct methylation signatures. Unfortunately, the success of this approach depends on the availability of high-quality reference data from other tumours for comparison, which is currently still a limitation.

The main goal of Prof Baumhoer's research is to establish a reliable methylation classifier for paediatric soft tissue and bone tumours. Over the last years, his research group has established an international network of experts to assemble well-characterized tumour samples as well as their methylome profiles. Their efforts have translated into the establishment of reliable methylation classes for over half of the bone and soft tissue tumours listed in the World Health Organization (WHO) classification. The data is included in a publicly available methylation classifier platform (www.epidip.org) and can be used free of charge.



Lead Researcher

Prof Daniel Baumhoer
University of Basel

An additional approach to enhancing tumour classification comes from determining chromosomal copy number profiles. High-grade sarcomas, for example, often show highly rearranged genomes, in contrast to benign tumours, which typically show fewer signs of genetic instability. This data can be derived from the same high-throughput sequencing technologies that are employed to perform methylation profiling (e.g., Illumina). Unfortunately, this technique is a lengthy (approx. two to three weeks) and expensive procedure, which hinders its implementation in resource-constrained settings. Hence, Prof Baumhoer and his research group are testing an ultra-fast and direct sequencing method using Nanopore devices. Using this cost-effective equipment, frozen tumour samples can be analysed to generate methylation and copy number profiles in under five hours, significantly reducing the time patients and treating physicians must wait to receive a diagnosis. In addition, this technique also seems promising using fine-needle aspiration material. Preliminary findings obtained from the analysis of aspirate samples are highly encouraging and demonstrate strong potential for future clinical application.

Overall, Prof Baumhoer's research efforts are contributing to improving diagnostic accuracy and objectivity for bone and soft tissue tumours, paving the way towards developing more targeted and individualized treatment strategies for children affected by rare tumours.

Image: Histological image of a sarcoma. Credit: Adobe Stock.

Research Programmes

Funding

The total research project funding across the various programmes since the launch of the BRCCH amounts to 37.7 million Swiss francs. Over the last year, 2,617,838 Swiss francs were spent on progressing BRCCH-funded research projects, which encompassed projects from the Principal Investigator Initiative (PII) and the Multi-Investigator Programme (MIP). The following sections give a brief description of the ongoing programmes and their projects.

Principal Investigator Initiative

The PII kicked off in 2022 to fund projects addressing current medical challenges faced by the paediatric population, with a particular focus on the Global South.

Six projects, involving fifteen lead researchers from the BRCCH's four partner institutions, were awarded four-year grants. These projects are collaborating with 38 international partners across 15 countries to find innovative solutions to the most pressing needs of children and adolescents. Major efforts have been made towards improving treatment options and treatment adherence. For example, the research consortium led by Prof Gabor Szinnai is developing a machine learning-driven model to improve the dosing and treatment of children afflicted with hyper- or hypothyroidism. Prof Edgar Delgado-Eckert, Prof Torsten Schmidth and Prof Elgar Fleisch are working on the design and implementation of a digital health application to optimize treatment adherence in paediatric patients with asthma in Romania. Moreover, Prof Daniel Paris and his research team are repurposing tuberculosis drugs for the treatment of Buruli ulcer, a necrotizing skin disease whose prevalence is very high among children from Cameroon. In terms of medical interventions, Prof Jennifer Keiser is conducting a cost-effectiveness analysis for the treatment of children with parasitic worm infections in Uganda, while Prof Sarah Moore and colleagues are integrating AI-driven tools to maximize the lifespan of insecticide-treated nets against malaria mosquitoes. Finally, Prof Dorothee Benz and Prof Marc Birhölzer are conducting a clinical study to identify the early signs of personality disorders in children across different ages.

The six PII projects underwent a mid-term evaluation at the end of 2024. During this process, international scientific experts assessed the progress, scientific quality and potential impact of the outcomes resulting from the six projects. All of the projects received positive evaluations, and the feedback from the external reviewers allowed the research consortia to strengthen their scientific approach and their potential impact.

Over the course of 2025, the BRCCH organized a seminar series covering the research topics developed by PII projects. Most of these events were broadcast online and recordings of the seminars can be found on our website.

Image: A social worker conduct a questionnaire interview to a school teacher in Kabale, Uganda in the context of a trial for the treatment of worm parasitic infections in children. Credit: Prof Keiser

Internship Programme

The Internship Programme was conceptualized in 2024 with the main goal of fostering capacity building and knowledge transference in paediatric digital health with scientists from low- and middle-income countries (LMICs). This programme is intended for researchers who wish to spend up to three months in a BRCCH-affiliated institution conducting research activities complementary to their home research projects and learning new methodologies in paediatric digital health. Currently in its pilot phase, the programme has thus far supported the following researchers:

- Dr Cecilia Herbozo (Cayetano Heredia University, Peru), who is developing a digital application to enhance the antenatal care training of healthcare providers in the highlands of the Peruvian Andes. She was hosted by Prof Daniel Mäusezahl (Swiss TPH), with whom she has initiated a research collaboration.

- Dr Cheah Fook Choe (University of Kebangsaan, Malaysia), who is engineering a Doppler ultrasound device to measure newborns' heart rates after the clamping of the umbilical cord. With the support of Prof Michele Magno (ETH Zurich) and his research group, Dr Cheah was able to successfully modify this medical device, whose functionality is currently being assessed in a clinical trial at several medical centres in Malaysia.

- Dr Grace Malhu (Ifakara Health Institute, Tanzania), a paediatrician whose main goal is to adapt digital clinical decision support algorithms for the diagnosis of children afflicted with tuberculosis. Hosted by Prof Fenella Beynon (Swiss TPH), her current collaboration is aimed at advancing the diagnosis and treatment of paediatric patients in Tanzania.

- Dr Evelyn Munayco Pantoja (Cayetano Heredia University, Peru), who is interested in developing an AI-based model for the automated detection of trachoma eye infection in children from Amazonia. Together with Prof Philippe Cattin (University of Basel), she has developed and trained an algorithm that can identify the presence of trachoma in eye pictures taken by smartphones.

During their internships in Basel, the participants had access to two educational courses to improve their knowledge in paediatric digital health: an online course on Foundations of Data Science, in which experts from ETH Zurich taught them the basis of designing machine-learning models for healthcare, and an in-person course on Foundations on Paediatric Digital Health, in which researchers in paediatric digital health from Swiss TPH described the foundations of designing, implementing and evaluating digital interventions for children and adolescents.

Multi-Investigator Programme

The MIP was launched in 2020 as the flagship of the BRCCH's research programmes. This initiative aims to forge multidisciplinary collaborations among our four partner institutions and international universities, with the ultimate goal of enhancing the likelihood of clinical translation and implementation worldwide. A summary for each project s presented in the following sections.

Image: Prof Cecilia Herbozo (Cayetano Heredia University, Peru) and Prof Cheah Fook Choe (Kebangsaan University, Malaysia), during their visit to the BRCCH offices in Basel on April 2025. Credit: BRCCH Management Office.

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

The first years of life are a cornerstone of child development, as they establish the foundations for all future learning, emotional and physical paediatric skills. However, more than 250 million children under the age of five are at risk of not realizing their full developmental potential. Many of these children reside in LMICs, facing early life adversities such as poverty and malnutrition, which hinder their development.

Presently, the most promising interventions for enhancing child health and well-being in LMICs involve home visiting, where healthcare staff or social workers assist parents in supporting the healthy development of their children. These programmes, however, are expensive and logistically challenging, making them unfeasible on a large scale in many resource-constrained settings.

Over the last years, digital tools for parents have begun to emerge. One such platform is Afini, an AI-based application that offers parental guidance with age-appropriate activities to support the development of young children.

To assess the impact, cost-effectiveness and scalability of Afini in LMICs, this research consortium conducted a cluster-randomized controlled trial involving 2,461 families with young children in the Peruvian highlands. The primary outcome of this trial was children's overall development at age 2.5 as measured by the Global Scales for Early Development Long Form. Secondary outcomes were parental engagement with the child and positive parenting behaviours alongside parents' reports of children's motor, cognitive, language and socio-emotional development.

Image: Two healthcare workers visit a family in San Marcos (Peru) as part of a home-visiting programme to support families during their children's early development. Credit: Stella Hartinger Peña.

Lead Researchers

Günther Fink
Swiss TPH

Daniel Mäusezahl
Swiss TPH

Within this study, families were randomly assigned to either a control group or a treatment group receiving digital support through the Afini platform. Moreover, the developmental skills of the children from the Afini group were also compared to those from a cohort receiving home visits from trained staff, which is considered the gold standard intervention for supporting vulnerable families.

The results of the trial show that both interventions, the digital parenting chatbot Afini and the traditional home-visiting programme, improved child development. Although children in families receiving home visits showed greater improvements on a standardized child development scale than those from families supported by Afini, the cost of the digital intervention was one-fifteenth the cost of in-person home visits. These findings underscore the feasibility of delivering high-quality parenting support through digital platforms in resource-constrained settings.

Complementing these activities, the research consortium developed and validated new digital measures to assess parenting and attachment. In addition, they created a data-credit incentive strategy to sustain caregiver engagement with digital interventions.

The project's results have already begun to influence the broader conversation around early childhood policies in the region. The research consortium has organized several meetings with governmental policymakers and programme leads—including those from Cuna Más and ORAS-CONHU—to include their digital intervention model in their ongoing family support strategies. Moreover, two lead researchers from this consortium have been invited to participate in the UNICEF panel on digital parenting interventions, ensuring a broader impact of this project's results in future early child development guidelines.

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

Image: Research consortium members during the presentation of the clinical study results in the "Congreso Internacional sobre Desarrollo Infantil Temprano y Entornos Sostenibles" conference that took place on the 10th-11th December 2025 and where the main outcomes of this project were presented Credit: Stella Hartinger Peña.

Lead Researchers

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Swiss TPH

Daniel Mäusezahl
Swiss TPH

Burden-Reduced Cleft Lip and Palate Care and Healing

Children born with cleft lip and palate—a gap in the upper lip and/or the roof of the mouth—often face significant challenges with feeding, breathing and dentition. This congenital craniofacial condition affects approximately one in 700 newborns worldwide, and there are currently no preventive measures available. Surgical repair, typically performed when the child is between six and twelve months of age, remains the only definitive treatment. Prior to surgery, infants commonly receive presurgical therapy via intraoral plates, which rest on the roof of the mouth to alleviate symptoms and optimize tissue conditions for surgical closure. Traditionally, these plates are made by hand from plaster casts, making the process highly technical, time-consuming and costly.

To address these challenges, this research consortium has combined advanced imaging, machine learning and 3D printing technologies to modernize presurgical cleft lip and palate care. Central to this effort is the development of AI-driven software that fully automatically computes patient-specific intraoral plates from 3D representations of an infant's palate, obtained through different digital acquisition workflows. These digital models can then be rapidly converted in intraoral plates using 3D printers, reducing manufacturing time.

In 2025, this research consortium pursued the clinical validation of this automated presurgical plate design pipeline at study sites in Basel (Switzerland) and Hyderabad (India). In a clinical study involving 60 infants, the smartphone-based approach was shown to be as effective as traditional methods, while significantly reducing both cost and production time. Notably, the automated workflow was associated with a 50% reduction in hospital visits during treatment and a substantial decrease in

Image: Dr. Prasad Nalabothu analysing the best individualised treatment for a patient with a palatal cleft in Hyderabad, India. Morphological change from before to after plate therapy is depicted on the computer screen (top to down, respectively). Credit: GSR Institute of Craniomaxillofacial and Facial Plastic Surgery.

Lead Researchers

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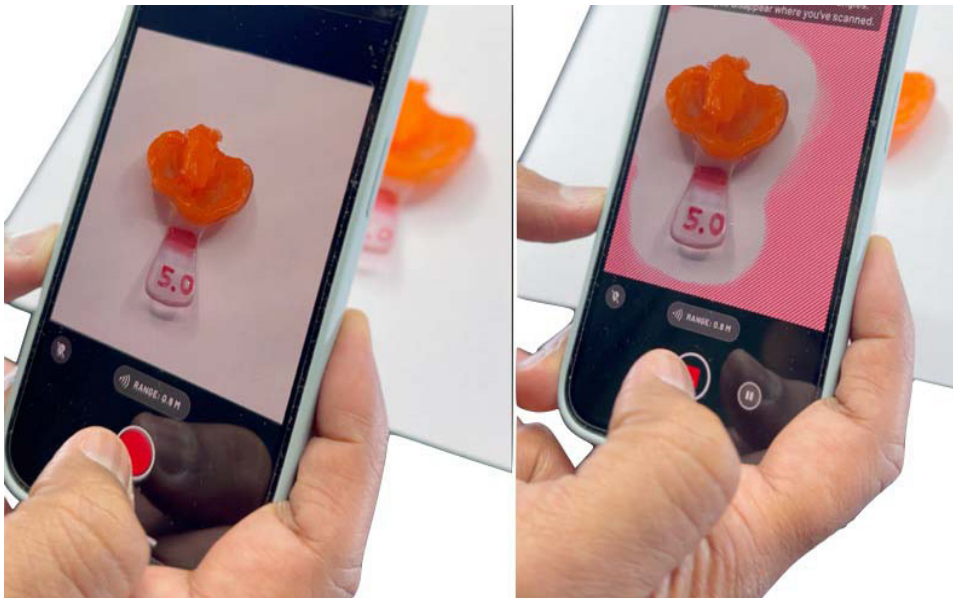
Barbara Solenthaler
ETH Zurich



manufacturing time, from two days to less than five hours. Clinical outcomes, including cleft width reduction and self-reported patient satisfaction, were comparable across both approaches, confirming the non-inferiority of the automated plate design methodology.

A further milestone was the establishment of smartphones as a reliable, low-cost alternative for intraoral scanning via two different methods. First, smartphones were used under real clinical conditions to produce 3D digitizations of the handmade intraoral impressions. This allowed researchers to seamlessly connect the automated plate design and manufacturing pipeline to conventional impression taking. Second, smartphones were used for contact-free 3D reconstructions of the palate using video-based acquisition. This approach relies on AI-driven 3D reconstruction methods capable of handling highly challenging input data characterized by uncontrolled camera motion and limited intraoral texture. To enhance the quality of the intraoral smartphone scan, the consortium designed and patented a self-retracting intraoral mirror.

Comparative preclinical analyses demonstrated that intraoral plates derived from smartphone-acquired videos achieved clinically relevant accuracy and robustness, reducing reliance on expensive clinic-based hardware and software.

Over the long term, this project has the potential to transform cleft lip and palate care by expanding access to high-quality, affordable treatment for thousands of children worldwide. By reducing healthcare costs and lowering the burden on families and healthcare systems, the initiative stands to significantly improve outcomes and quality of life for affected children and their families.

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).

Image: Impression scanning for the treatment of an unilateral complete cleft lip and palate. The scanning process begins from the top, covering as many views of the object as possible until no more stripes appear, following the app instructions.Credit: Maren Roche

Lead Researchers

Andreas Müller
University Hospital Basel and University of Basel

Barbara Solenthaler
ETH Zurich

Living Microbial Diagnostics to Enable Individualized Child Health Interventions

The gut microbiome, or in other words, the billions of microorganisms colonizing the human large intestine, is acquired in the first years of life and is shaped over time as the diet becomes more complex. It is integral to child health, as it contributes to food digestion and the development of children's immune and central nervous systems. Hence, monitoring the gut microbiome is critical to ensuring that millions of children reach their full developmental potential, even though non-invasive monitoring methods have not yet been developed.

Over the last years, this consortium has successfully used CRISPR-based technology to engineer a bacterium capable of traversing the gastrointestinal tract of animals while sensing, remembering and reporting on the gut environment it encounters. As the engineered bacterium travels through the intestine, its gene expression changes depending on the environment it encounters.

When used in specific-pathogen free mice fed with different perturbed diets, the engineered bacterium detected fluctuations in certain micronutrients such as iron or zinc, whereas it remained insensitive to vitamin B12, folate or changes in short-chain fatty acids produced via fibre fermentation. This set of experiments, among others, enabled the team to establish ten marker genes indicative of iron and zinc concentrations. Changes in the expression of these genes can be used to infer micronutrient concentration with an accuracy of 75% and 81% for each compound respectively. These findings serve as a proof of concept in the diagnostic validation of this technique.

Image: An image displaying future healthcare technology to create probiotic bacteria to improve digestive health. Credit: Adobe Stock.

Lead Researchers

Randall Platt
ETH Zurich

Dirk Bumann
University of Basel

Uwe Sauer
ETH Zurich

In a complementary approach, this consortium has optimized the reporting abilities of the engineered bacterium by creating two new temperature-inducible recording systems and improving the algorithm underlying the read-out gene expression analysis. All these approaches have been patented, bringing this non-invasive diagnostic tool one step closer to its clinical translation.

An additional focus of this project is the analysis of the impact of malnutrition and related disorders on shaping the gut microbiome in the first years of life. To determine the risk factors in the vertical transmission of an impaired gut microbiota, this consortium has been collecting longitudinal samples from mothers and babies living in Zimbabwe and Switzerland. By analysing and comparing faecal and breast milk samples, among other variables, they will be able to determine which factors are responsible for certain paediatric outcomes such as stunted growth. The outcome of this study could help inform nutritional guidance to improve gut microbiome health in breastfeeding mothers and, in turn, improve child growth.

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

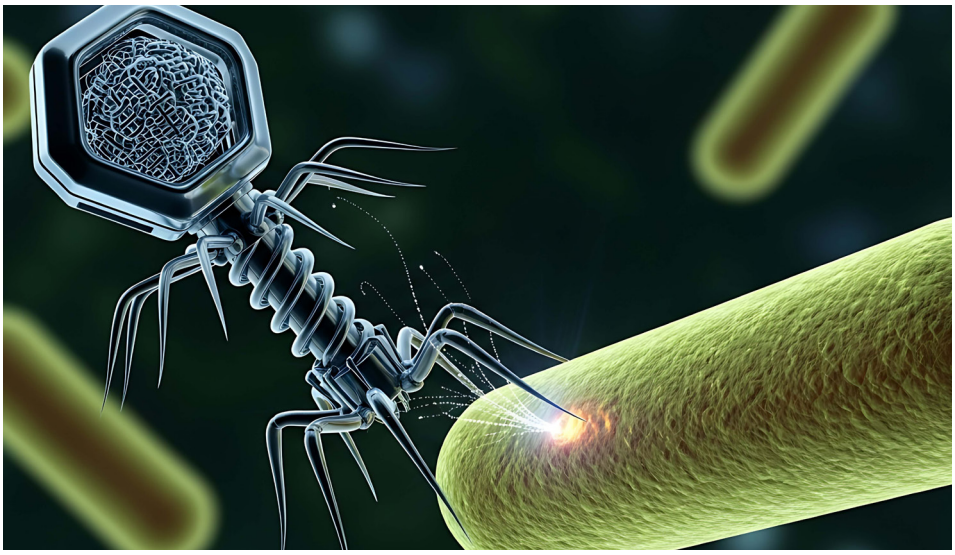
Image: A transcriptional recording techniques by CRISPR spacer acquisition from RNA, an integral methodology for this project. Credit: Adobe Stock.

Lead Researchers

Randall Platt
ETH Zurich

Dirk Bumann
University of Basel

Uwe Sauer
ETH Zurich



Precision Microbiota Engineering for Child Health

The gut microbiome is increasingly being recognized as a hidden organ based on its contribution to human health; it contributes to nutrient production, eliminates toxins such as ammonia and can regulate the immune response. In addition, the microbial communities act as a honed ecosystem protecting the host from infection by preventing pathogenic bacteria from colonizing the lumen. Consequently, disruptions in gut microbiota composition are associated with dysregulated physiological functions, including chronic inflammation, autoimmune diseases and neurological disorders. Despite its importance, our ability to precisely and durably alter the composition and function of the gut microbiome remains limited to date.

Over the past five years, the main objective of this research consortium has been the development of bioengineering tools and strategies capable of modulating microbiome community dynamics. A key initial step towards long-lasting microbiome interventions was the systematic identification and classification of Escherichia coli (E. coli) strains based on their surface polysaccharide composition. The resulting large-scale genotype–phenotype database, together with kTYPr, an open-source bioinformatics tool developed to query this resource, has allowed the researchers to identify novel molecular targets present in pathogenic bacteria residing in the gastrointestinal tract. These targets can be exploited to render otherwise elusive pathogens susceptible to vaccine-mediated targeting.

This knowledge established the foundation of a "vaccine-enhanced competition" strategy—a strain-replacement approach designed to prevent pathogen invasion and subsequent infection in the gastrointestinal tract. Using animal models, the researchers demonstrated that the combined administration of an oral vaccine and a fast-growing, non-pathogenic competitor strain effectively excluded Salmonella from the gut. The oral vaccine promoted antibody-mediated recognition and clearance of the invasive pathogen, enabling the harmless competitor to occupy its ecological niche within the microbial community.

Image: A bacteriophage attacking a bacterium. Credit: Adobe Stock.

Lead Researchers

Emma Slack
ETH Zurich

Johannes Bohacek
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Médéric Diard
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Shinichi Sunagawa
ETH Zurich

Viola Vogel
ETH Zurich

Ferdinand von Meyenn
ETH Zurich

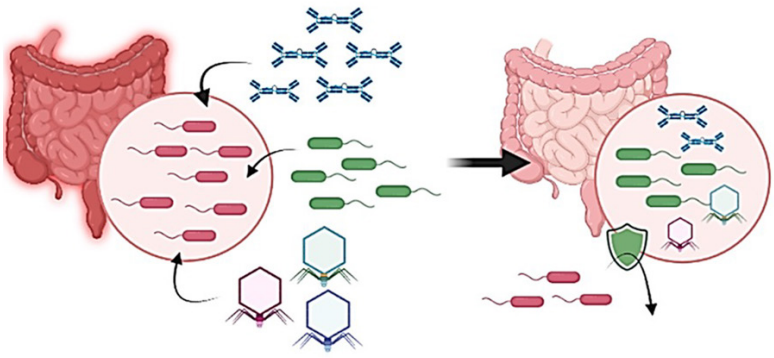
These findings have broad medical implications, particularly for the prevention of neonatal infections caused by E. coli, such as sepsis and meningitis. In the case of neonatal meningitis, E. coli K1 strains are the leading cause of this infection and are notoriously difficult to target due to the similarity between the K1 capsule and host-derived polysaccharides. To overcome this challenge, the research consortium developed a strategy entailing a cocktail of bacteriophages that use the K1 capsule as their receptor. Phage attachment to the bacterium triggers capsule loss, thereby increasing bacterial susceptibility to vaccine-mediated clearance. When combined with the administration of a harmless bacterium, this approach effectively suppressed E. coli K1 colonization and reduced transmission to neonatal mice. This set of proof-of-concept experiments validated the feasibility of the intervention, which was patented and now forms the scientific core of Baxiva AG, an ETH-derived start-up company.

Precision microbiome engineering is also highly relevant for children born with inherited disorders who are unable to detoxify ammonia from their body. The high ammonia levels present in the blood of these children can traverse the blood-brain barrier and impair brain development. This research consortium has demonstrated that in these patients, the gut microbiome is markedly altered, and experiments in mice have revealed an inverse correlation between microbial composition and the severity of neurological disease. These findings challenge the prevailing paradigm that the gut microbiome exacerbates disease by increasing the body's ammonia levels. Furthermore, they highlight the importance of promoting microbiome growth in these patients, which goes against the antibiotic therapy often prescribed to them. To ensure that the project outcomes are included in future clinical guidelines, this research consortium is closely collaborating with physicians from University Children's Hospital Zürich specializing in the treatment of these patients.

Overall, this project is pioneering a precision microbiome engineering framework with direct translational impact, enabling novel preventive and therapeutic strategies for severe paediatric diseases and accelerating their path towards clinical and commercial implementation.

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 schematic representation of the "vaccine-enhanced competition" strategy coupled with a bacteriophage for clearing a pathogenic bacterium from the gut microbiome. Credit: Louise Larsson.



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Research Outputs and Communications

Over the last year, BRCCH-funded researchers continued to publish their findings in scientific journals, providing evidence-based information for public health decisions and reaching lay audiences with media communication. A summary of the BRCCH facts and numbers is displayed below.

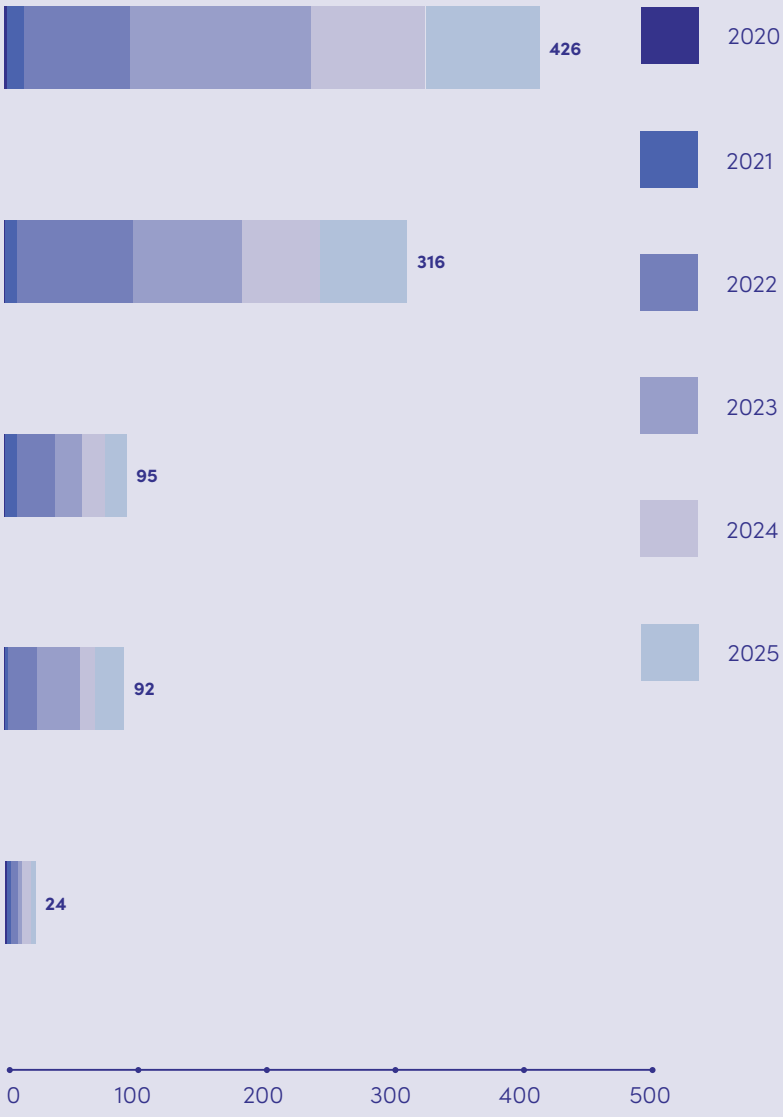
426 Research Presentations (Oral talks and poster presentations)

316 Publications and Datasets (Scientific articles, reviews and datasets)

95 Public Engagement and Outreach Activities (Communications with the public)

92 Capacity-Building Activities (Education and training activities for scientists)

24 IPs and Spin-Offs (Patent Applications and Companies established)



Additional activities

Inaugural Lecture of Prof Na Cai

On 17 November 2025, Prof Cai presented her past and current research activities in a BRCCH-organized event that took place at the Department of Biosystems Science and Engineering (D-BSSE) at ETH Zurich. In her lecture entitled "Genetics of Depression: From Statistical Associations to Molecular Understanding," she described the main challenges underpinning the genetic causes of major depressive disorders. A recording of her BRCCH inaugural lecture can be found **here.**

Image: Prof Na Cai presenting her research activities during her BRCCh Inaugural Lecture. Credit: BRCCH Management Office.

Research Seminars

As in previous years, in 2025 the BRCCH hosted seminars to highlight the outcomes of its research projects. These events are accessible online to ensure the largest possible reach. The topics of these presentations included:

- **"Personalising Dosing for Children with Thyroid Diseases"** featuring BRCCH researchers Prof Gabor Szinnai (UKBB), Dr Britta Steffens (UKBB) and Freya Bachmann (University of Konstanz, Germany). Through their presentations, the speakers addressed the challenges faced by clinicians when treating children experiencing hypo- or hyperthyroidism. Moreover, they described how machine-learning-based algorithms can support clinicians in prescribing an optimal treatment.

Image: Philippe Cattin presenting his research activities in the framework of the BRCCH project ViALLIN at the Swiss Tropical and Public Health Institute. Credit: BRCCH Management Office

- **"Feasibility and Economics of Improved Child Deworming with Albendazole-Ivermectin,"** including BRCCH-funded researchers Prof Jennifer Keiser, Prof Peter Steinmann and Prof Fabrizio Tediosi, all based at Swiss TPH. During this seminar, the speakers highlighted the barriers and facilitators encountered when administering this combined treatment in schools in Uganda. In addition, they presented an economic analysis comparing the costs of a single vs double treatment for parasitic worm infections.

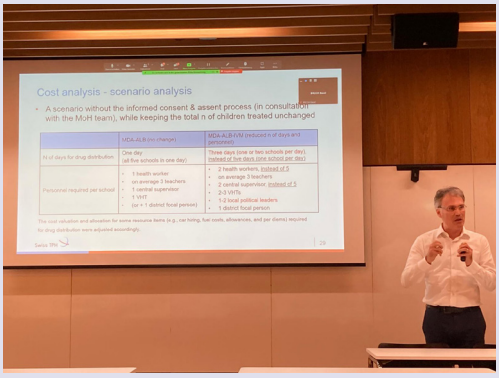
- **"Evidence in Focus: Using Visual Analytics to Shape the Future of Insecticide-Treated Net Procurement,"** with the BRCCH-funded researchers Prof Sarah Moore (Swiss and Tropical Public Health Institute), Prof Philippe Cattin (University of Basel) and Emmanuel Mbuba (Swiss and Tropical Public Health Institute). The speakers delivered a comprehensive description on how integrating computational methods with insecticide-treated nets can enhance the efficiency of this intervention, which is the most frequently used method to prevent malaria infection. A recording of the seminar can be found in **here.**

Image: Prof Delgado-Eckert during his BRCCH seminar introducing the ALEX project at the Biozentrum. Credit: BRCCH Management Office.

- **"Digital Approaches in Respiratory Research and Clinical Practice,"** featuring BRCCH researchers Prof Edgar Delgado-Eckert (University of Basel), Prof Ioana M. Ciuca (Victor Babes University of Medicine and Pharmacy, Romania) and Prof Mihai Craiu (Carol Davila University of Medicine and Pharmacy, Romania). At this event, the experts described the promising potential of supervised machine learning and AI-automated imaging recognition in the treatment of children and adolescents experiencing asthma, pneumonia or other respiratory diseases.

- **Bridging Early Detection and Innovation in Adolescent Mental Health: Current Research & Emerging Digital Solutions,"**with BRCCH researchers Prof Dorothée Bentz (University of Basel), Prof Marc Birkhölzer (University Psychiatric Services Bern) and Ana Gregorec (University Medical Center Maribor, Slovenia). The three experts guided the audience through the mental health challenges currently experienced by children and adolescents worldwide, including personality disorders. They also provide new insights into how virtual reality tools are becoming part of the diagnosis and treatment of individuals experiencing emotional distress. A recording of the seminar can be found **here.**

Image: Prof Fabrizio Tediosi presenting a cost-analysis during his talk at the STPH. Credit: BRCCH Management Office.



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