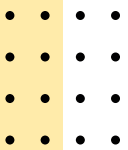
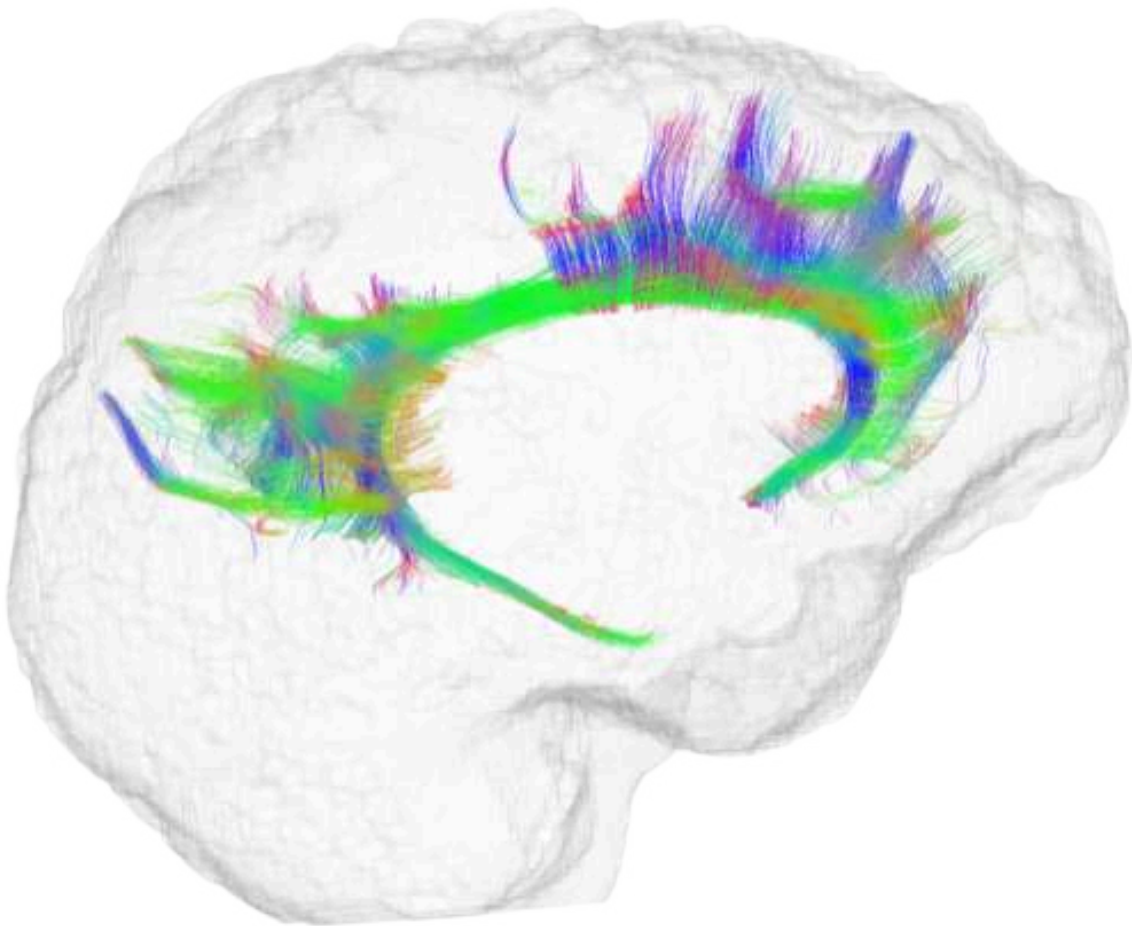


RESEARCH CENTER FOR CLINICAL
NEUROIMMUNOLOGY AND NEUROSCIENCE BASEL

RC2NB

ANNUAL REPORT 2024



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OUR VISION

ADVANCING SCIENCE, ENHANCING LIVES

Improving the life of people with MS and other neurological diseases through the development and integration of innovative tools that comprehensively characterize the disease process, facilitate the development and implementation of better treatments and enable personalized disease management. The Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB) is a leading destination for cutting-edge research and clinical innovation. As an academic-industry initiative, we are committed to advancing Neuroimmunology and Neuroscience, specifically focusing on understanding and treating Multiple Sclerosis and other neuroimmune diseases.

In collaboration with the MS Center at the University Hospital Basel, RC2NB provides an unparalleled, interdisciplinary approach to patient oriented research and care. We work closely with other local, national and international clinical departments and institutions, ensuring that our research and care benefit from the latest diagnostic advancements and specialized treatments.

MESSAGE FROM CEOs

2024 HAS BEEN A YEAR OF FURTHER CONSOLIDATION BUT ALSO GROWTH AND NEW SCIENTIFIC ACHIEVEMENTS FOR RC2NB AS A LEADING RESEARCH CLUSTER IN CLINICAL NEUROIMMUNOLOGY AND NEUROSCIENCE.

Converging evidence from different research areas and from recent large clinical studies further underlined the need for more comprehensive, granular, and specific assessment of neuroimmune diseases. This encourages us in pursuing the sometimes stony path of systematic validation and implementation that leads from discovery to clinical translation. This Annual Report summarizes main achievements as we proceed along the four RC2NB workstreams:

In the development of new digital biomarkers for monitoring clinical progression, we completed enrollment of the *dreaMS validation study 1* with



275 MS patients and 50 healthy controls. A first interim data look confirmed that we are on track and we advanced the development of analytical tools in collaboration with our partners at INDIVI Ltd. Administrative and technological preparatory work for our international multicenter study in Europe and North America, *dreaMS Validation Study 2*, took longer than expected also because we needed to compensate effects of Roche's decision in early 2024 to stop their complete FLOODLIGHT program in MS.

Neurostatus-UHB Ltd continued its role in quality control of standardized clinical assessments by providing over 10,500 expert reviews for randomized controlled trials (RCTs). The now published *SMARTCARE study* showed that trained healthcare professionals were equally reliable in performing standardized Neurostatus-EDSS assessments as neurologists, a step towards better quality in decentralized clinical studies. In the *eCluster project*, we apply AI methods to large sets of Neurostatus eEDSS data aiming to achieve more granular (sub)gradings in the EDSS score range of 4.5 to 6.5.

In *Workstream 2*, the *ThINK Basel group* achieved significant milestones, leading to high-impact publications in *JAMA Neurology*, *Annals of Neurology*, and *Neurology*. They applied advanced quantitative MRI to identify remyelination/repair activity in a longitudinal setting in vivo as well as in cortical lesions postmortem. Postmortem imaging also allowed the discovery of new sources of contrasts in MS brains, such as astrocytes as well as areas of active remyelination, which were imaged with cellular-spatial resolution. In the investigation of the pathophysiology of progression independent of relapses, the group develops and validates AI-based methods for translating novel findings into clinical practice.

The *Swiss MS Cohort Study* and *fluid biomarker group* further elucidated the role of glial fibrillary acidic protein (GFAP) and combined GFAP/serum neurofilament light chain (sNfL) as predictors of MS progression. GFAP as a marker of microglial activation and damage was more and independently predictive of progression independent of relapse activity (PIRA) whilst sNfL as marker of axonal damage was robustly predictive of inflammatory activity. These findings were published in leading neurology journals such as *Annals of Neurology* and *JAMA Neurology*.

In *Workstream 3*, the *Clinical Neuroimmunology group* completed its flagship study on the mechanistic connection between Epstein-Barr virus (EBV) and lesion formation in MS.

The *Experimental Neuroimmunology group*, in collaboration with an international consortium, demonstrated that BAFF elevation following B- cell depletion therapy provides neuroprotection in MS and EAE (*Science Translational Medicine* (2024)). Together with the fluid biomarker group they showed that NfL and GFAP have a role as monitoring biomarkers for MOGAD and AQP4-NMOSD, with findings published in *JAMA Neurology*.

In *Workstream 4*, the SNSF funded Investigator initiated pragmatic trial MULTISCRIP had a jumpstart, recruiting more than half of planned participants within 2024. The Pragmatic Evidence Lab provided essential methodological support including the publication of the Delphi study that established consensus on a standardized framework for integrating sNfL into treatment decision algorithms, fostering shared decision-making between MS patients and physicians. The team is now preparing to expand the MULTISCRIP learning system, with a focus on new markers and new drug treatments for disease progression as a model for translating research into care.

CLINNOVA, a flagship project of the University of Basel and University Hospital Basel (USB), achieved a major milestone in 2024 with the enrollment of its first patient in Basel, marking a significant step towards collaborative data-driven healthcare.

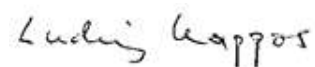
Structurally, Professors *Jens Kuhle* and *Tobias Derfuss* were jointly appointed as clinical professors of Neuroimmunology, strengthening the links between RC2NB, the Neurology Clinic, and the University of Basel.

Lars Hemkens was promoted to associate professor (Titular Professor) in Clinical Epidemiology. In 2024 we officially established a *Pragmatic Data Science Center (PDSC)* to coordinate and further enhance our expertise in statistics, deep learning, and clinical trials. Whilst *PD Johannes Lorscheider* left RC2NB and USB by December 2024 to accept a permanent leading position at Rehaklinik Rheinfelden, we welcome *Dr Jannis Müller*, who is best prepared to step in as research group leader for dreaMS and a new member of the management group of RC2NB as of January 2025.

To conclude the year, we hosted the *MS Info Day*, an event organized for our patients and their relatives, to inform about recent advances in diagnosis and treatment and to share milestones achieved thanks to their invaluable collaboration.

In its four Workstreams and in international collaborations the RC2NB team authored or co-authored 118 peer-reviewed original papers, editorials, and reviews. Several of our scientific collaborators completed their Master or PhD in 2024 or received prizes at scientific meetings. *Jens Kuhle* was awarded with the prestigious Sobek Prize in recognition of his exceptional achievements in developing blood-based biomarkers and leading the Swiss MS Cohort Study.

Throughout this transformative journey, we at RC2NB are deeply grateful for the continued trust and support of the University Hospital, the University, national and international research organizations, corporate sponsors, and all our valued partners.



LUDWIG KAPPOS

CEO



CRISTINA GRANZIERA

CO-CEO

BOARD OF TRUSTEES

Foundation Board of Trustees

Prof Christiane Pauli-Magnus - Chair of the Board, Co-Head, Department of Clinical Research, University Hospital Basel, **Dr med Werner Kübler, MBA** - CEO University Hospital Basel), **Prof Primo Schär** - Vice-Rector Research, University of Basel, **Prof Eva Scheurer** - Dean Medical Faculty, University of Basel. *The Board of Trustees held two meetings, on April 5, 2023 and December 20, 2023.*

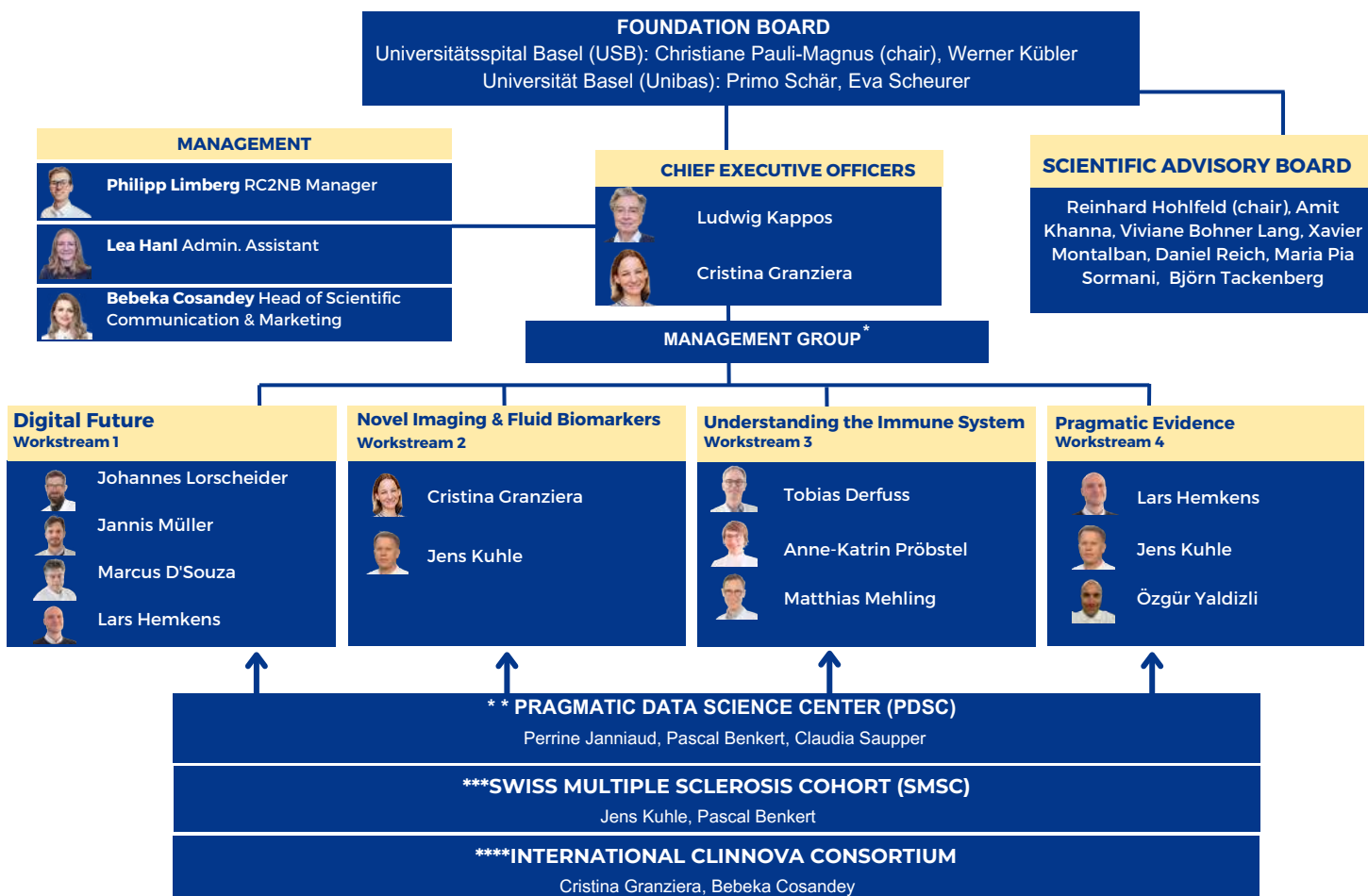
Scientific Advisory Board

Prof Reinhard Hohlfeld - Chair, Munich, Germany, **Dr Viviane Bohner Lang** - Patient representative, Allschwil, Switzerland, **Dr Amit Khanna**, Basel, Switzerland, **Prof Xavier Montalban**, Barcelona, Spain, **Prof Daniel Reich**, Bethesda, United States of America, **Prof Maria Pia Sormani**, Genova, Italy, **Prof Björn Tackenberg**, Basel, Switzerland. *The international RC2NB Scientific Advisory Board (SAB) meets annually and independently reviews the work and provides advice to the RC2NB. The annual in-presence meeting was held on October 29th, 2024.*

QUOTE FROM THE SCIENTIFIC ADVISORY BOARD REPORT IN 2024

"The SAB is impressed by the productivity of all workstreams, as evidenced by numerous publications in high-quality journals - particularly welcomes the increase in joint publications co-authored by PIs from different work streams. This reflects the benefits of the research environment in Basel that fosters translational MS research (including patient cohorts, expertise in clinical trials, novel tools for clinical phenotyping as well as outstanding expertise in neuroimaging of MS tissue, fluid biomarkers and immunological monitoring of therapy)."

RC2NB GOVERNANCE BODIES



*Management group members: Derfuss Tobias, D'Souza Marcus, Granziera Cristina, Hemkens Lars, Kappos Ludwig, Kuhle Jens, Lorscheider Johannes, Müller Jannis, Pröbstel Anne-Katrin.

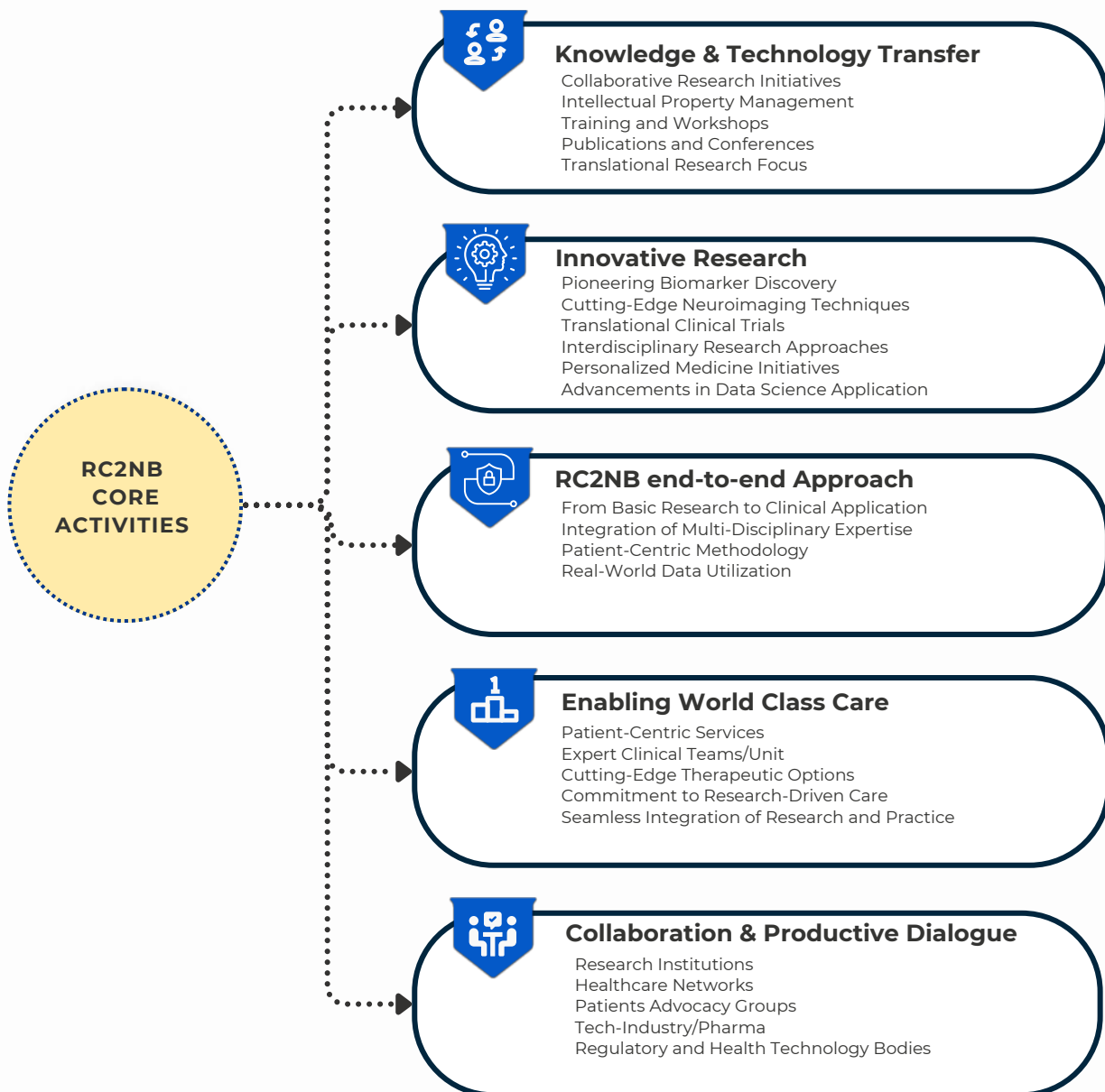
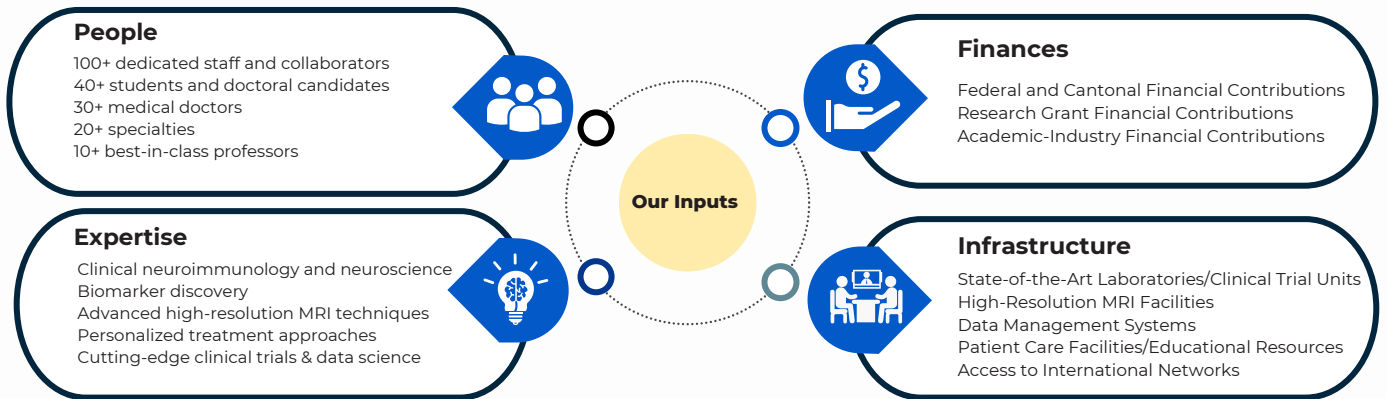
**PDSC is responsible for coordinating data analysis, artificial Intelligence, machine learning, in partnership with USB-IT, DKF, SciCore, Indivi and further external partners, s. p. 24.

***SMSC is a Swiss wide prospective high quality cohort, currently including > 2000 participants in 7 centers, s. p. 15-16

****CLINNOVA drives healthcare digitalization by building data infrastructure and ensuring interoperability across systems in 4 countries, s.p.23.

How RC2NB

RC2NB: ADVANCING



Creates Value

SCIENCE, ENHANCING LIVES

RC2NB SUCCESS FACTORS



RC2NB OUTPUTS IN 2024



* Over the past years, from 2019 to 2024.



SCIENTIFIC ACHIEVEMENTS 2024

RC2NB ANNUAL REPORT 2024

Aleksandra Maleska processing biosamples in the Lab.

FOUR WORKSTREAMS - ONE VISION

Four interconnected workstreams collaborate toward the shared goal of RC2NB. These workstreams bring together interdisciplinary research teams that work both within and across their respective areas to drive innovation. Their efforts focus on developing advanced tools for monitoring the health of persons with MS and

other neuroimmune and neurodegenerative diseases, gaining deeper insights into the complex disease process, enabling more precise and personalized disease management, and ultimately discovering more effective treatments to improve patient outcomes.



WORKSTREAM 1: DIGITAL FUTURE

Research Group Leaders



Prof Cristina Granziera
dreaMS



PD Dr Johannes Lorscheider
dreaMS (until Dec. 2024)



Dr Jannis Müller
dreaMS (from Jan. 2025)



PD Dr Marcus D'Souza
Neurostatus-UHB



Prof Lars Hemkens
dreaMS

The mission of Workstream 1 is to advance digital assessment methods for MS care and research.

With “dreaMS”, we aim to establish and validate smartphone and wearable-based digital measures for MS.

The group received a starting grant by Innosuisse – Schweizerische Agentur für Innovationsförderung – and additional funding by grants from Roche, Novartis and others to the Foundation for Clinical Neuroimmunology and Neuroscience Basel.

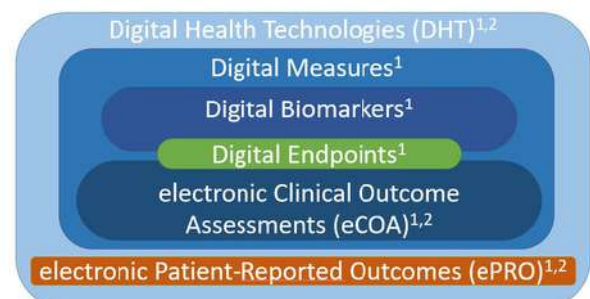


Figure 1. Word cloud with the most frequently used terms in the analysed digital biomarker(s) definitions. From: Macias Alonso AK, Hirt J, Woelfle T, et al. Definitions of digital biomarkers: a systematic mapping of the biomedical literature. *BMJ Health Care Inform.* 2024;31:e100914. doi: 10.1136/bmjhci-2023-100914

In 2024 we completed recruitment of our *Swiss-wide validation study 1* (VS1, NCT05009160). The recruitment of a total of 275 participants with MS and 50 healthy volunteers was made possible through support by the Swiss MS Cohort Study (SMSC) centers at the University Hospital Zurich, the University Hospital Lausanne (CHUV), the EOC Lugano and the Cantonal Hospitals St. Gallen and Aarau. The participants are followed up for at least 2 years. 30 participants who completed the 2-year core study have already entered a 2-year extension study. By including only participants from the SMSC, we have ideal conditions to compare the validity and sensitivity for change over time of the new digital metrics derived from dreaMS with the high-quality and well-standardized clinical, laboratory and imaging markers of disease severity and progression obtained in the SMSC.

An important part of the dreaMS App is our in-house developed suite of cognitive games (Figure 3). To investigate the relative difficulty between levels, reliability, practice effects, and ability to measure change in performance over time, we conducted the CoGames study with 76 healthy volunteers (Pless S. et al., *J Neurol*, in press).

All difficulty levels of all games reached our predefined cut-offs for test-retest reliability, and we obtained data allowing to quantify the difficulty differences between levels and practice effects. Overall, the results of CoGames support our assumption that these adaptive, digital, and gamified cognitive tests can be used as reliable and well-accepted assessment- and monitoring tools in MS but also in other diseases affecting cognitive functions.



(1) EMA: <https://www.ema.europa.eu/en/documents/other/questions-answers-qualification-digital-technology-based-methodologies-support-approval-medicinal-en.pdf>
(2) FDA: <https://www.fda.gov/media/155022/download>

Figure 2. Overview of terminology used by EMA and FDA. Digital health technologies obtain digital measures, which include digital biomarkers and electronic clinical outcome assessment (eCOA). Digital biomarkers and eCOAs can both provide digital endpoints. EMA, European Medicines Agency; FDA, Food and Drug Administration. From: Macias Alonso AK, Hirt J, Woelfle T, et al. Definitions of digital biomarkers: a systematic mapping of the biomedical literature. *BMJ Health Care Inform.* 2024;31:e100914. doi: 10.1136/bmjhci-2023-100914

The second key element in our scientific validation strategy is the *international Validation Study 2*. This multinational cohort study will include about 600 participants across Europe and North America and aims to replicate the results of Validation Study 1 with a stronger focus on patient-centered outcomes and optimal generalizability of findings.



Figure 3. Screenshots of dreaMS cognitive games

The start of this investigator initiated study (planned for end of 2024 is now delayed to Q3 2025 due to unforeseen administrative delays and our decision to replace modules of FLOODLIGHT (Roche) that are complementing dreaMS modules in VS1. As FLOODLIGHT tests won't be available anymore for VS2, we decided to replace them by integrating new equivalent tests.



dreaMS team, from left to right: Wölfle T, Phavanh V, Wiencierz A, Lacalamita M, Pless S, Sala, R, Müller J, Kolb S, Limberg P. For the full team, please refer to the members list on pages 32 to 34.

Neurostatus-UHB AG

Neurostatus-UHB AG operates as a 100% subsidiary of the University Hospital and, as of December 2024, has a team of 25 employees. In 2024, the Neurostatus-EDSS was licensed to 94 active phase II/III MS trials, of which one third is using the digital version that has been shown to significantly improve consistency of assessments. (Neurostatus-eEDSS). This digital version is also used in the dreaMS validation studies 1 and 2.



Neurostatus team. Lower row: Lee J, Waiz C, Cerda Fuertes N, Boos L, Cysin A, D'Souza M, Garcia E, Tschirky M. Upper row: Njuguna S, Demirtzoglou A, Forman B, Hug G, Fricker E, Kel J, Wunderlin S. For the full team, please refer to the members list on pages 32 to 34.

For industry sponsored clinical trials Neurostatus-eEDSS is implemented in collaboration with established electronic clinical

outcome assessment (eCOA) companies that are granted non- exclusive licenses.

In addition to the guidance and substantial support during implementation in the environments of these eCROs, the team of Neurostatus-UHB Ltd is responsible for the continuous quality control and provided more than 10'500 individual expert-reviews for RCTs in 2024.

The SMARTCARE study was completed and showed that trained healthcare professionals are able to assess the Neurostatus-EDSS with equal accuracy as Neurologists. (Mallucci G et al., MSJ 2024). This is an important step towards better quality in decentralized clinical studies.

Even a seasoned scale as the EDSS, first described in 1955 and 1983, may be subject to further improvement: In the eCluster project we apply AI methods to large sets of Neurostatus eEDSS data aiming to achieve more granular (sub)gradings in the EDSS score range of 4.5 to 6.5 that -in the current version- is dominated by ambulation and does not take into account changes in other functional domains (M. Greselin, MSJ, in press).



Scan me to access Neurostatus website.

WORKSTREAM 2: INNOVATIVE IMAGING AND ANALYSIS OF BODY FLUIDS

Research Group Leaders



Prof Cristina Granziera
Translational Imaging in
Neurology - ThINK Basel



Prof Jens Kuhle
Swiss MS Cohort Study and
Laboratory of Clinical Neuroimmunology

ThINK Basel: Innovative imaging



Translational Imaging in Neurology (ThINK) Basel is a collaborative, multi-principal investigator initiative that operates at the intersection of translational research and cutting-edge neuroimaging. The group is affiliated with the University of Basel's Department of Biomedical Engineering, the Neurology Department at University Hospital Basel, and the Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB).

ThINK Basel is composed of five principal investigators (Prof Cristina Granziera, Prof Dr Regina Schläger, PD Dr Katrin Parmar, PD Dr Athina Papadopoulos, and Prof Dr Oezguer Yaldizli) and their teams, amounting to 46 members.

Within this framework, **Prof Cristina Granziera** has the lead and coordination of the entire group as well as the direct supervision of a dynamic team of 26 professionals, including master's and Ph.D. students, postdoctoral fellows, senior scientists, and research staff, all working collaboratively to advance neurology and neuroimaging research.

Our main research focus is the understanding of multiple sclerosis (MS) pathophysiology, the identification of biomarkers of MS progression and therapy response, the development of new computational models of MS disease impact and evolution as well as the investigation of mechanisms of structural remodeling/regeneration within the central nervous system of patients with MS. To achieve

these goals, we exploit the sensitivity and specificity of advanced quantitative magnetic resonance imaging and modern analysis methods including classical machine-learning techniques and deep-learning networks. The group is funded through a grant from the Swiss National Science Foundation (SNSF), the Hasler Foundation, the "Stiftung zur Förderung der gastroenterologischen und allgemeinen klinischen Forschung", intramural funding of the University of Basel and corporate research grants. In 2024, we achieved some major milestones in the understanding of mechanisms underlying clinical worsening in people with MS as well as in the exploration of novel biomarkers for MS diagnosis and in the identification of novel methods to assess focal remyelination and novel features of MS pathology in postmortem studies. We have substantially contributed to advance the procedures for MS diagnosis by exploring the diagnostic value of cortical lesions and central vein sign in a large MAGNIMS study involving more than 1000 MS patients (Cagol A. et al., JAMA Neurol 2024).

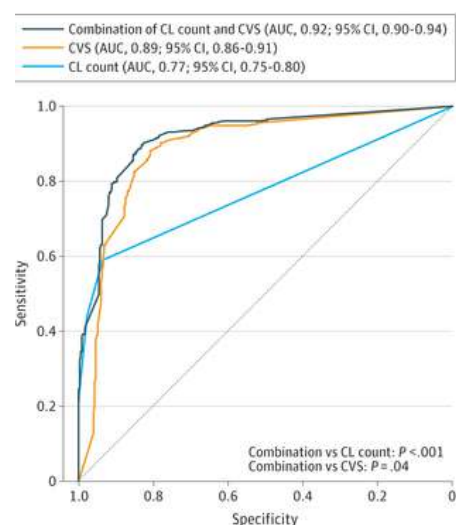


Figure 4. Combination of Cortical Lesions (CLs) and Central Vein Sign (CVS) for Discrimination Between Multiple Sclerosis/Clinically Isolated Syndrome and Other Diagnoses. Image from Cagol A. et al., JAMA Neurol. 2024.

Moreover, we have applied novel approaches based on the combination of multishell diffusion and magnetization transfer imaging that allowed us to identify lesion classes based on repair and damage features over time (Sanabria G, et al., *Annals Neurol* 2024) as well as based on myelin characteristics as derived by applying the chi separation method to quantitative-susceptibility mapping and multi-echo T2 data (Müller J. et al., *Neurology* 2024). In both studies, we have also obtained that the proportion of repaired lesions was related to the patients' disability (Figure 4). In addition, we are pursuing the explorations postmortem both at 3T and 9.4 T in collaboration with the neuropathology team in Göttingen and with the medical physics team in Freiburg (Germany). In this context, we have developed ultra-high-resolution protocols at 9.4 T that have cellular resolution, as well as made novel observations related to the distribution and contribution to the diffusion signal of activated astrocytes (Callegari I. et al, *ECTRIMS* 2024 and Gkotsoulis D. et al., *ECTRIMS* and *ISMSRM* 2024).



The ThInk group at ECTRIMS 2024. From left to right: Greselin M, Chen X, Spagnolo F, Cagol A, Prof Granziera C, Giacomelli E, Bar Zohar N, Ocampo Pineda M. For the full team, please refer to the members list on pages 32 to 34.

PD Dr Athina Papadopoulou leads a team of seven doctoral and post-doctoral researchers, which focuses on the investigation of the retina and visual pathway in MS and other neuroinflammatory disorders as well as on the study of headache and central pain.

Applying OCT, quantitative MRI and evoked potentials in collaboration with the lab of electrophysiology and the team of Prof C. Granziera, the team investigates structural-functional associations along the visual pathway in people with MS (pwMS).

We showed that structural damage at the synapse-level of the thalamic Lateral geniculate node (LGN) may contribute to functional visual damage (Papadopoulou A. et al, *Clinical Neurophysiology*, 2024).

Furthermore, the group investigated in 2024 the role of retina markers to predict progression independent of relapses, so called "PIRA" (progression independent of relapse activity), in pwMS.

In the "REMIND" study (Retinal Markers In Neurological Diseases), which is funded by a SNF-"Ambizione" grant to Athina Papadopoulou, neuronal loss in the retina was related to increased rates of progression independent of relapses - (PIRA) (Burguet F. et al, *ECTRIMS* 2024). Moreover, In collaboration with the Department of Sport, Exercise and Health (Prof H. Hanssen), the team analyses retinal vessel diameter as measure of the impact of vascular comorbidities and as a marker of disability and treatment effects. The team also explores associations between OCT-derived retinal measures and imaging and body fluid biomarkers. In this context, we found a close relationship between neuronal retinal loss and serum Glial Fibrillary Acidic Protein levels (sGFAP) (Sellathurai et al., *ECTIRMS* 2024), while analysis using advanced MRI is ongoing.

Prof Regina Schlaeger leads a research team of 7 post-doctoral fellows, doctoral students and master students, which focuses on the investigation of motor neuron diseases and other genetic, neurodegenerative and inflammatory diseases of the spinal cord and cerebellum. The team is funded by several grants from private foundations as well as corporate research grants.

Currently several prospective imaging studies are ongoing that evaluate novel sequences and MR approaches developed by our partners in MR physics (Prof Olivier Bieri, Magnetic Resonance Physics & Methodology and PD Dr Santini, Basel Muscle MRI).

To validate these novel MR-sequences the team also conducts post-mortem studies in collaboration with the research groups of Prof Eva Scheuer and PD Dr Claudia Lenz, University of Basel as well as with the team of C. Granziera.

In 2024, Prof Regina Schlaeger's team described the lateral corticospinal tract sign – a novel MRI marker for amyotrophic lateral sclerosis that distinguishes ALS from other forms of motor neuron diseases (Wendebourg et al., *Radiology* 2024). Based on rAMIRA imaging, a sequence developed by Matthias Weigel and Prof Oliver Bieri at the department of Radiological Physics, the group also investigated spinal cord gray and

white matter atrophy and its association to clinical disability in ALS (Wendebourg et al., European Journal of Neurology, 2024) and spinal muscular atrophy (Kesenheimer et al., Journal of Neurology 2025).

Last, in collaboration with PD Dr Santini's group and funded by the Swiss National Science Foundation (219674) the group also started working on novel multiparametric MRI methods for Myotonic Dystrophy Assessment and Management.

Prof Özgür Yaldizli leads a team of three research associates and two master students. In addition to their contribution to Multiscript (see WS 4) the group is investigating the role of the choroid plexus and is part of an international collaboration supported by an ERA-NET NEURON grant to study the significance of the choroid plexus in multiple sclerosis and chronic pain.

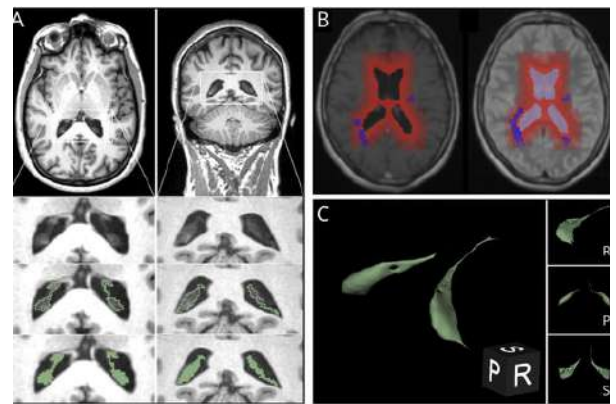


Figure 5. Choroid Plexus Segmentation and White Matter Parcellation. Image from Neurol Müller J. et al., Neurol Neuroimmunol Neuroinflamm. 2022.

Finally **PD Dr Katrin Parmar** is an associate member of ThInK Basel. She currently works as senior consultant neurologist in Reha Rheinfelden. In this context, she plans studies using digital and imaging biomarkers for rehabilitation purposes.

Clinical Neuroimmunology and Swiss MS Cohort: Biomarkers from Bench to Bedside

The Clinical Neuroimmunology Laboratory led by **Prof Jens Kuhle** focuses on the discovery, development, and validation of body fluid biomarkers and is responsible for the blood and cerebrospinal fluid biobank of the Department of Neurology and the national coordination of the SMSC.

Results of projects funded by the Swiss National Science Foundation and the National MS Society (USA) were published in more than 10 publications that consolidate and deepen our knowledge about NFL and demonstrate the added value of serum glial fibrillary acidic protein (sGFAP) for personalised medicine.

Expanding its activities into neuromyelitis optical spectrum disorders (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), an international consortium led by the Clinical Neuroimmunology Laboratory is establishing novel biomarkers for these diseases, allowing for a more expedited diagnosis and eventually more timely start of therapy.

Swiss MS Cohort Study (SMSC)

The SMSC is meanwhile in its 12th year of existence providing high quality clinical and imaging data, and biofluid samples from more

than 13'800 time points for translational medicine research and the definition of novel precision medicine tools. SMSC has become the key resource for clinical and translational research projects at RC2NB, the MS Centre at the University Hospital Basel and within numerous national and international collaborations. More than 40 publications authored or co-authored by the Clinical Neuroimmunology Laboratory from late 2023 and 2024 are based on data obtained in the SMSC.



Jens' Lab team, from left to right: Kuhle J, Rodriguez Calvo M, Oechtering J, Zadic A, Maleska A, Vilchez Gomez Juan F. For the full team, please refer to the members list on pages 32 to 34.

Biofluid Markers: neurofilament light chain and glial-fibrillary acidic protein

The Clinical Neuroimmunology Laboratory has pioneered in the past years the development of neurofilament light chain (NfL) as the first blood-based biomarker up to clinical applicability for personalised medicine in MS (Benkert et al., *Lancet Neurology*, 2022; Abdelhak et al., *Lancet Neurology*, 2023); by November 2024 more than 240.000 NfL measurements have been correlated by researchers and physicians using our web based application for the normative database for adults (<https://shiny.dkfbasel.ch/baselInflreference/>). We recently launched a similar for use in children and young adults (<https://shiny.dkfbasel.ch/baselInflreference-for-kids/>).

These tools improve the utility of sNfL levels for MS patients and facilitate the detection of correlations with actual clinical and MRI defined disease activity, response to treatment, as well as their prognostic power for later clinical and MRI outcomes, including therapeutic response. Based on these results, NfL has become a reference measure in individual patient workup, as well as in clinical trialling of MS and other neurological diseases.

However, there was a lack of a biomarker reflecting more specifically the neuro-

degenerative aspect of MS usually manifesting clinically as continuous disability accumulation ('progression').

This gap has recently been narrowed by the results of our studies of glial-fibrillary acidic protein (GFAP) as a second blood-based biomarker for MS (Swiss National Science Foundation grant 320030_212534, 10.2023-10.2027). GFAP in blood has a stronger capacity than NfL to prognosticate quantitatively the pace of 'smouldering MS' or PIRA (progression independent of relapse activity) (Figure 6) and is a predictor of treatment effects on progressive disease pathology, currently the most important unmet need in MS (Benkert et al., *Annals of Neurology* 2024).

The longitudinal pattern of serum levels (Figure 7) of these two biomarkers illustrate that they depict different pathophysiological pathways. It is, therefore, likely that the combination of NfL and GFAP becomes a standard measure for the development of drugs specifically targeting progression, as well as for personalised disease management.

These results confirm and expand on a prior study (Meier et al, *JAMA Neurology* 2023) and demonstrate that a single measurement after one year of therapy start delivers a robust prediction of the future course of disease.

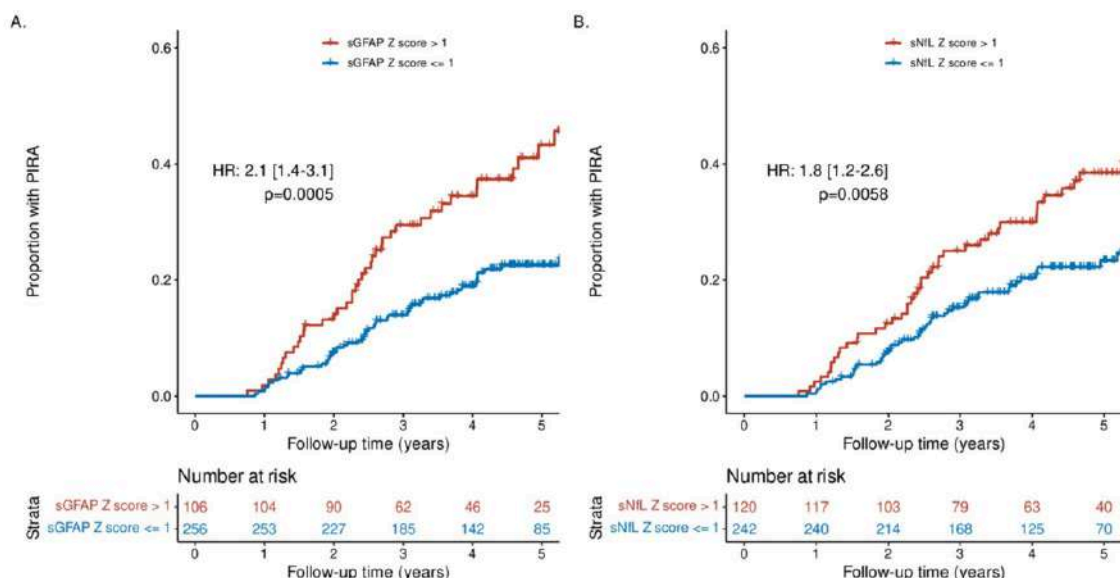


Figure 6. Kaplan–Meier curves showing the proportion of patients experiencing future PIRA when having high (Z score > 1) versus low (Z score ≤ 1) biomarker levels of sGFAP (A) and sNfL (B) at index sample. Patients with a sGFAP Z score > 1 (≥84.1st percentile) at index sample (median 1 year after BCDT start) were at 2.1-fold risk of a future PIRA event versus those with sGFAP Z score of ≤ 1 (HR: 2.1 [1.4–3.1], p = 0.0005); accordingly, patients with a sNfL Z score > 1 showed 1.8-fold increased risk to develop PIRA compared to patients with a sNfL Z score ≤ 1 (HR: 1.8 [CI: 1.2–2.6], p = 0.0058). HR, hazard ratio; PIRA, progression independent of relapse activity; sGFAP, serum glial fibrillary acidic protein; sNfL, serum neurofilament light chain.

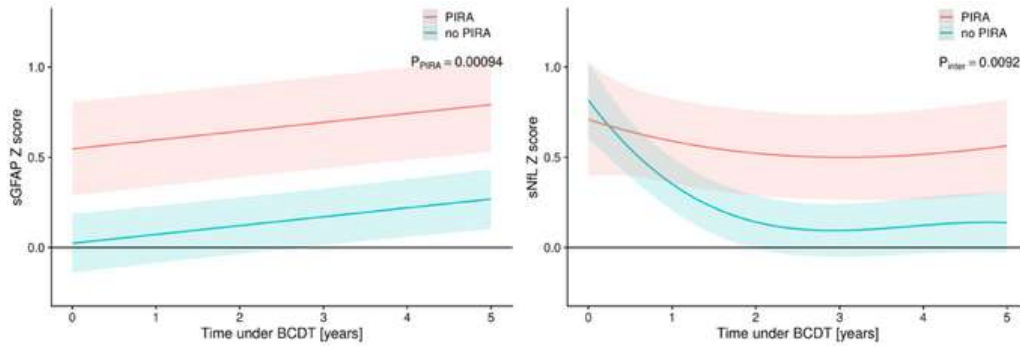


Figure 7. Longitudinal dynamics of sGFAP (A,C) and sNFL (B,D) Z scores under BCDT in relation to PIRA. Marginal effects on predicted biomarker Z scores over time. Z score: 0 represents the mean biomarker concentration in control persons. Models are adjusted for age and EDSS at BCDT start and for recent relapse (<90 days before sampling). Left: sGFAP Z scores steadily increased over time by 0.49 Z score units/10 years ($p < 0.0001$) in both PIRA and non-PIRA patients, whereas there was no difference in slopes between the 2 groups (pinteraction PIRA*follow-up time = 0.44). However, Z scores were 0.52 units higher in patients developing PIRA during follow-up ($p = 0.0009$). Right: No difference in sNFL Z scores was observed in patients with versus those without PIRA at start of BCDT ($p = 0.38$). However, the dynamics of sNFL over time differed between these groups (pinteraction PIRA*follow-up time = 0.0028): in patients without PIRA, sNFL strongly decreased by 0.92 Z score units/10 years ($p < 0.0001$), whereas in those with PIRA, Z scores remained stable over time. BCDT, B-cell depleting therapy; PIRA, progression independent of relapse activity; sGFAP, serum glial fibrillary acidic protein; sNFL, serum neurofilament light chain.



Vilchez Gomez Juan Francisco, in the Lab.

Novel cerebrospinal fluid markers for the differential diagnosis of acute stage NMOSD and MOGAD vs MS

We have recently identified granulocyte activation(GAM) and astrocyte damage (ADM) markers as a novel biomarker set for the differential diagnosis of acute stage neuromyelitis spectrum disorders (NMOSD) and MS (JNNP 2023, figure 8). The detection of anti aquaporin 4 autoantibodies in NMOSD is the diagnostic gold- standard. However, these antibodies score negative in approximately 20% of patients overall and their laboratory turnaround time does not match the need for a seamless start of therapy in acute stages. Further, as GAM are likely effector molecules of acute neural damage in NMOSD, they are the first biomarkers that correlate with the actual degree of disability (Figure 6), unlike the antibodies targeting aquaporin-4.

Higher levels of these markers were found in NMOSD, an astrocytopathy, than in MOGAD, an oligodendrocytopathy. As a result of these studies, we were able to propose, for the first time, a flow chart of biomarker analysis that

allows the reliable differentiation of NMOSD, MOGAD and MS, largely independent of the detection of autoantibodies. Our laboratory leads an international consortium to further validate these findings and establish an easy-to-use assay platform for these biomarkers that can also be applied outside of specialised academic centres, expediting the initiation of adequate therapy.

Similarly, GAM also correlated with disability in MOGAD (MSJ 30 (3), pp.1180-1181, 2024 and Neurology 109, 7(Suppl) P9.004, 2024). Measuring levels of the astrocyte damage markers GFAP and S100B might help to differentiate MOGAD and NMOSD.

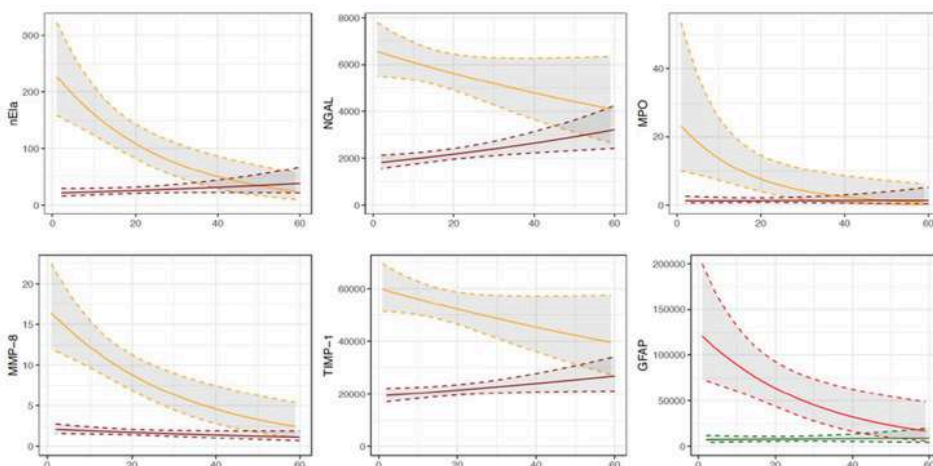


Figure 8. Modelled kinetics of biomarker levels in NMOSD and MS in function of days after disease exacerbation. Biomarker values are in pg/mL. Values on x-axis show days after disease exacerbations. Dotted lines determine 95% CI, based on all patients. In acute stages, NMOSD nEla, MPO, MMP-8, and TIMP-1 are increased vs MS. Note that GFAP serves here as control target, being increased as an astrocyte damage marker known to be increased in NMOSD. MMP-8, matrix metalloproteinase 8; MPO, myeloperoxidase; nEla, neutrophil elastase; NGAL, neutrophil gelatinase-associated lipocalin; TIMP-1, tissue inhibitor of metalloproteinase-1 (Leppert D, Watanabe M, Schaedelin S, Piehl F, Furlan R, Gastaldi M, Lambert J, Evertsson E, Fink K, Matsushita T, Masaki K, Isobe N, Jun-ichi K, Benkert P, Maceski A, Willemse E, Oechtering J, Orleth A, Meier S, Kuhle J. Granulocyte activation markers in cerebrospinal fluid differentiate acute neuromyelitis spectrum disorder from multiple sclerosis. (2023). Journal of Neurology, Neurosurgery, and Psychiatry, 94:726-737)



Scan us to access the THINK, SCMC and MS Center websites.









WORKSTREAM 3: RECORDING AND UNDERSTANDING THE DYSREGULATED IMMUNE SYSTEM

Research Group Leaders



Prof Tobias Derfuss
Cellular and Molecular
Neuroimmunology



Prof Anne-Katrin Pröbstel
Experimental
Neuroimmunology



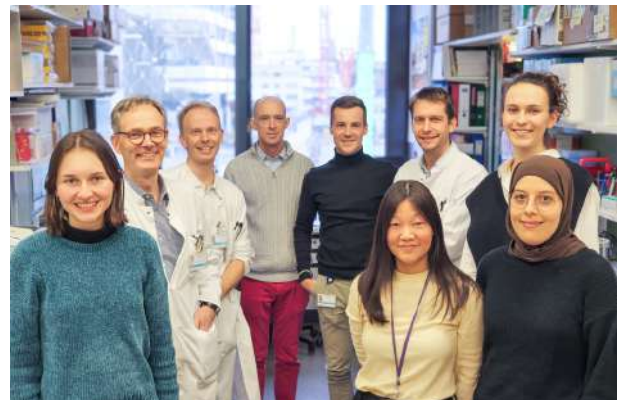
Prof Matthias Mehling
Immunosenescence, Protective
Immunity under DMT

The Clinical Neuroimmunology Lab (Prof Derfuss) studies the biology of multiple sclerosis and related diseases from two approaches. The top-down approach depends on observational studies of immunologic parameters in patients, both in response to treatment and in the natural history of the disease. The bottom-up approach involves *in vitro* and *in vivo* experimental modeling of plausible hypothetical mechanisms to explain the observations. The group is funded by SNF project grants, a Sinergia grant, as well as by the Swiss Personalized Health Initiative and grants from industry and private foundations.

First results of the top-down approach obtained in the SNF-Sinergia-funded collaboration with immunologists and computational biologists in Zürich (Nr. 10.000.065/ CRSII—222718) were published in January 2024 (Ulutekin C, Galli E, Schreiner B. *Cell Rep Med.* 2024). This paper analyzes the effect of B cell depletion on the immune landscape using high-dimensional single-cell immuno-phenotyping.

We will continue this approach to characterize the particular peripheral immune cell populations that are involved in the pathogenesis of MS. In one project, we will analyze the combined effects of sequential immunotherapies. Moving forward, we will focus more on the role of EBV, with one approach continuing to use the high dimensional, high throughput techniques that have been central to the collaboration thus far, and the “bottom up” approach using humanized mice to study the interaction between EBV infected B cells and the CNS *in vivo*.

In 2024, the group completed its flagship study of the mechanistic connection between Epstein-Barr virus (EBV) and lesion formation in MS



Tobias' Lab Team, from left to right: Sakiri E, Prof Derfuss T, Diebold M, Sanderson N, Schneider M, Galli E, Nadišauskaitė R, Chang H, Raach Y. For the full team, please refer to the members list on pages 32 to 34.

(paper under review). A clear association between previous EBV infection and MS incidence has been well established by several groups over many years, but a mechanistic explanation for this dependency is still lacking.

By combining data from our autoreactive B cell screening pipeline with results from experiments with transgenic mouse models, and patient biopsy data obtained in collaboration with the department of Neuropathology in Freiburg/Br, we assembled a model that posits an initial CNS infection as a driver of immune cell infiltration, combined with the EBV-driven expansion of an auto reactive B cell clone. Results from animal modeling have revealed that autoreactive B cells that enter the CNS during localized inflammation are - in the absence of cognate T cell help - normally efficiently eliminated by activation-induced cell death.

The EBV protein LMP1 provides a surrogate for this T cell signaling, and leads to the survival of autoreactive, CNS-infiltrating B cells, the secretion of autoantibody, and localized demyelination. Figure 9 is a graphical abstract summarizing methods and findings.

The experimental Neuroimmunology Group's (**Prof Pröbstel Anne-Katrin**) current research focuses on three main topics: (I) deciphering microbial-immune cell crosstalk in MS, (II) decoding pathogenic B cell and antibody profiles in MOGAD, (III) identifying microbial and immune signatures associated with treatment (non-) response.

Achievements in 2024 include: (1) In a joint effort with the groups of Prof Gommermann (Toronto) and Prof Zipp (Mainz) and contributions from Jens Kuhle (Workstream 2), we demonstrated that elevation of BAFF following B cell depletion therapy offers neuroprotection in MS and EAE (Wang*, Lüssi*, Neziraj*, Pössnecker* et al. Science Translational Medicine, 2024) pointing towards a potential novel mode of action of anti-CD20 depleting therapies through immune regulatory responses.

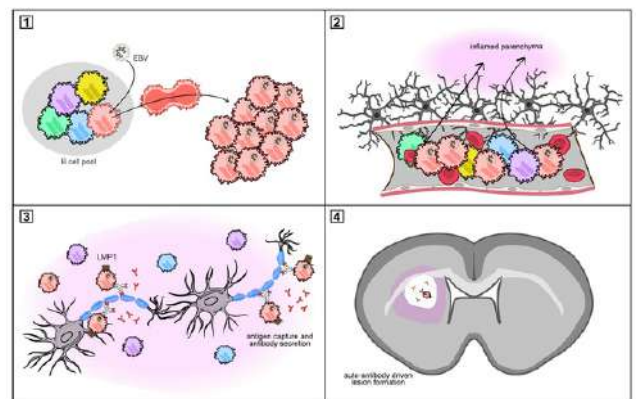


Figure 9. Schematic description of the newly proposed model explaining the role of Epstein Barr virus in initiating lesion formation in MS. (1) A self reactive, naive B cell is rescued into a memory-like clone by infection with the virus. (2) A CNS infection with a second, unrelated, neurotropic virus or other CNS insult provokes the influx of immune cells, including B cells from the autoreactive clone. (3) Autoreactive B cells are activated by interaction with cognate antigen, and saved from activation-induced cell death by the EBV protein LMP1. (4) Activated autoreactive B cells survive in situ and secrete autoantibodies, leading to demyelinated lesion formation. From Kim, Schneider et al., submitted.

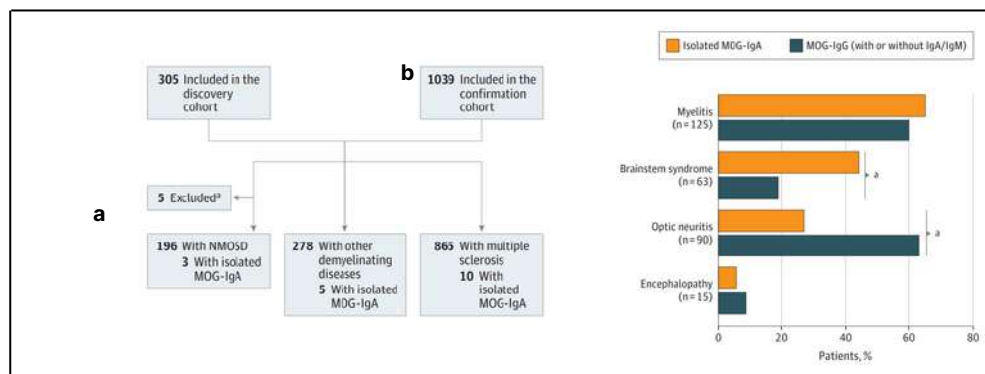


Figure 10. MOG-IgA characterizes a subgroup of patients with central nervous system demyelination. (a) Flowchart of patients in the discovery and confirmation cohort who were screened for MOG-IgA, MOG-IgG, and MOG-IgM. (b) Frequency of disease manifestations for patients with isolated MOG-IgA and MOG-IgG.

(2) In experimental models Lena Siewert and Elisabeth Pössnecker identified antigen-specific activation of gut originating immune cells as a driver of autoimmune neuroinflammation with implications for the role of the microbiome in triggering autoreactive immune response in MS patients (Siewert et al., under revision).

(3) In a multicenter effort led by Anne-Katrin Pröbstel in collaboration with Jens Kuhle, we investigated the role of NfL and GFAP as a monitoring biomarker in MOGAD and AQP4-NMOSD (Kim SH, Gomes ABAGR, et al. JAMA Neurol. 2024).



Pröbstel's Lab, from left to right, upper row to lower row: Prof Pröbstel AK, Flammer J, Neziraj T, Gutzwiller S, Cullen Baumann P, Berve K, Scherhag F, Lipps P, Gutzwiller J, Wetzel N, Kulsvehagen L, Bohnen L, Schäfer V, Pössnecker E, Lerner J, Lecourt AC. For the full team, please refer to the members list on pages 32 to 34.

Unraveling the Role of Immunosenescence in Multiple Sclerosis.

In the past year the research group of **Prof M. Mehling (Translational Neuroimmunology)** at DBM has focused on understanding the interplay between immune aging and the disease course of multiple sclerosis (MS), particularly in relation to cytomegalovirus (CMV) infection and disease-modifying treatments (DMTs). As part of the Swiss Multiple Sclerosis Cohort (SMSC) study at the University Hospital Basel, the group investigated T cell senescence profiles and their functional characteristics across various treatment groups. In a cohort of 229 persons with MS (pwMS), they characterized T cell subsets using multiparameter flow cytometry and analyzed biomarkers such as neurofilament light chain (NfL) and senescence-associated secretory phenotype (SASP) factors.

These findings highlight CMV as a significant driver of T cell senescence, independent of DMT.

Notably, we observed that CMV reactivity is linked to a less severe disease course, while CMV-antibody negative individuals exhibit stronger correlations between T cell senescence and disease activity. Additionally, the data obtained reveal distinct age-related T cell profiles across individuals treated with different DMTs, with DMF-treated patients showing differential associations between markers of T cell senescence and disease activity depending on CMV status. These findings underscore the importance of personalized therapeutic strategies that consider both immunosenescence and anti-viral reactivity. Ongoing research aims to further elucidate these complex interactions to allow for personalized MS treatment strategies improving patient outcomes.

WORKSTREAM 4: PRAGMATIC TRIALS AND REAL-WORLD EVIDENCE

Research Group Leaders



Prof Lars Hemkens
Senior Scientist Neurology



Prof Özgür Yaldizli
Consultant Neurologist



Prof Jens Kuhle
Swiss MS Cohort Study and Laboratory
of Clinical Neuroimmunology

Workstream 4 continues to provide a comprehensive framework for translating innovation into clinical research and care by developing methodologies and infrastructures that assess clinical meaningfulness and patient benefits.

These efforts focus on generating high-quality real-world evidence, leveraging RC2NB's interdisciplinary expertise, and fostering pragmatic, decentralized, and remote clinical trials. This integration enhances the seamless translation of research findings into routine care.

Flagship Initiative: MultiSCRIPT embedded in the Swiss MS Cohort

MultiSCRIPT (MultipleSclerosis Pragmatic Platform Trial), an investigator-initiated study exemplifying RC2NB's mission of seamlessly integrating research into care. The effectiveness and clinical meaningfulness of innovative treatment strategies are continuously evaluated with pragmatic research methodologies. As a transformative learning care system launched in 2022 and funded by the Swiss National Science Foundation, MultiSCRIPT is embedded within **the Swiss MS Cohort (SMSC), led by Prof Jens Kuhle** (s. Workstream 2).



Pragmatic Trial Team, from left to right, Louise Chaboud, Prof Lars Hemkens, Dr Perrine Janiaud.

SMSC is a long-standing, high-quality cohort study characterized by standardized procedures and robust, high quality real-world data collection. It provides the ideal foundation for merging pragmatic randomized trial methodology with real-world evidence generation.

MultiSCRIPT's ultimate goal is to establish personalized treatment approaches, directly embedded into routine care for persons with multiple sclerosis (MS).

Led by **Prof Oezguer Yaldizli (co-PIs Prof Jens Kuhle, Prof Lars Hemkens, and Prof Chiara Zecca from Lugano, scientific coordination by Dr Perrine Janiaud)**, MultiSCRIPT's first cycle evaluates a biomarker monitoring strategy using serum neurofilament light chain (sNfL) values for personalized treatment decisions compared to standard care in a randomized trial design. This approach aims to improve either the proportion of patients achieving no evidence of disease activity (NEDA3) or their health-related quality of life.

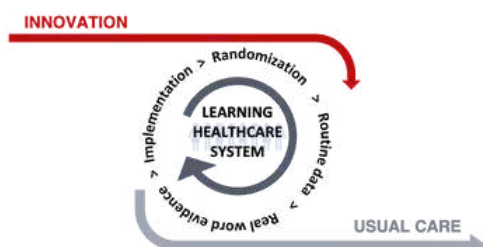


Figure 12. By merging randomized trial methodology with real-world cohort data collection, we aim to create a learning healthcare system where innovations are continuously evaluated and directly translated to usual care in a sustainable study environments and data structures.

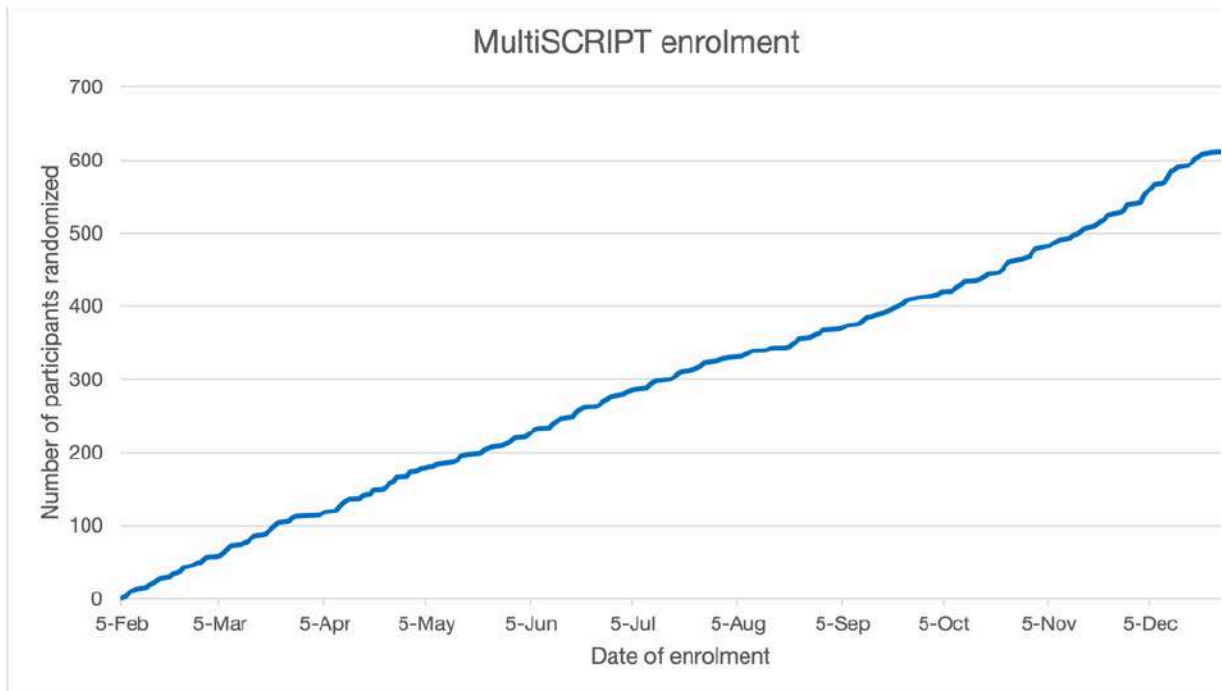


Figure 11. MultiSCRIPT recruitment rate
 The MultiSCRIPT enrolled its first participant February 5th, 2024 and in less than a year recruited 590 participants.

If proven superior, the strategy will establish a new standard of care, paving the way for future cycles to evaluate other innovative diagnostic or treatment approaches. After its full integration into the SMSC, which enabled streamlined patient randomization using digital tools for data collection and optimized consent and quality-of-life measurement processes,

MultiSCRIPT rapidly recruited nearly 2/3 of the target sample size in less than a year (Figure 11), with additional SMSC centers coming on board. This remarkable achievement is a testament to the commitment and collaboration of SMSC partners and participating in the SMSC (90 % acceptance rate of eligible pwMS).

Scan us to access the Pragmatic Evidence Lab and Multiscript websites.

PRAGMATIC EVIDENCE LAB

 MultiSCRIPT



CLINNOVA-MS BASEL: DIGITAL PRECISION MEDICINE



Prof Cristina Granziera
Principal Investigator



Dr Bebeka Cosandey
Lead Scientific Project Manager



International Clinnova Consortium Team, Strasbourg January 2024

2024 has been a transformative year for Clinnova – Federating Digital Medicine in Europe, a flagship project of the University of Basel, and funded with CHF 4 million by the Basel-Stadt Kanton. This initiative aims to redefine healthcare by creating a data-driven ecosystem that focuses on personalized medicine, improves patient care, accelerates biomedical research, and develops patient-focused applications.

As a key component of this international consortium, our team in Basel is leading the Multiple Sclerosis use case and has established the groundwork ensuring that the technical, regulatory, and clinical foundations are in place, and building a robust study infrastructure. A significant milestone occurred on December 10, 2024, when the first patient was enrolled, officially marking the start of the study in Basel. The team's efforts were also highlighted at the Multiple Sclerosis Info Day at the University Hospital Basel, where researchers engaged directly with patients and demonstrated the real-world impact of their work.

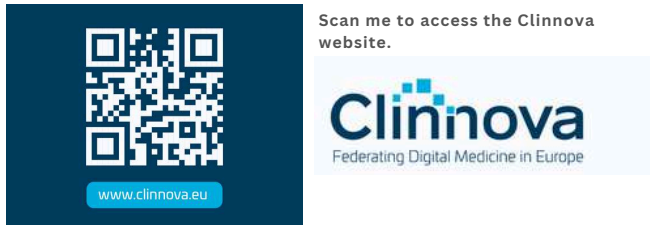
The team driving this initiative forward includes Prof Cristina Granziera, who leads Clinnova-MS Basel; Dr Bebeka Cosandey, who oversees strategic coordination; and Tanja Stoll, whose hands-on involvement ensures seamless study operations and patient care.

As we enter 2025, the focus will be on scaling patient recruitment and

harnessing real-world data to fuel federated learning, a cutting-edge approach to AI-driven research. The project's Data Integration Centers (DICs) play a crucial role in this vision, offering a secure, interoperable, and scalable infrastructure based on open-source technologies. These DICs ensure that health data is standardized, transformed into meaningful insights, and used responsibly to drive scientific discovery while safeguarding patient privacy.

What sets Clinnova apart is its federated learning framework. Instead of sharing raw patient data, each site retains full control while contributing to the collective training of AI models. This privacy-preserving approach is establishing a new standard in secure, data-driven healthcare innovation, not just for multiple sclerosis but for a wide range of diseases.





For those eager to learn more, the newly launched Clinnova consortium website (www.clinnova.eu) provides in-depth insights into our research, ongoing projects, and future directions.



Clinnova Basel team, from left to right: Dr Bebeko Cosandey, Prof Cristina Granziera, Tanja Stoll

PRAGMATIC DATA SCIENCE CENTER (PDSC)



Dr Perrine Janiaud
Head of PDSC



Claudia Saupper
Data architect



Pascal Benkert
Head of SMSC datacentre,
senior statistician

With the wealth of expertise comes wealth of data

As we thrive to continuously improve patient care, data drives our innovation and research. RC2NB has a unique portfolio of clinical, laboratory, imaging, and digital data. The PDSC was launched last quarter of 2024 and serves as a connection point for all data generated in the different workstreams. Working closely with the data center of the SMSC (led by Dr Pascal Benkert), THINK (led by Prof Cristina Granziera), and external academic and industry partners, we work to ensure the interoperability of our diverse data sources, the harmonization in data definition and the optimization of data collection minimizing patients' research burden.

By leveraging the data and expertise from all workstreams, including clinical researchers, AI experts, data scientists and statisticians, the PDSC aims to strengthen knowledge sharing across workstreams towards the identification, validation and implementation of biomarkers and novel endpoints for clinical trials.



Beyond the data, the PDSC aspires to be a hub of innovation, fostering an environment for junior researchers to exchange ideas and explore new research avenues that they may not have been previously considered.



RC2NB ANNUAL REPORT 2024

RC2NB EVENTS 2024

Scientific Advisory Board (SAB) Research Meeting 2024

RC2NB AT ECTRIMS 2024: ADVANCING MULTIPLE SCLEROSIS RESEARCH

From September 18 to 20, 2024, many of us participated in the Congress of European Treatment and Research in Multiple Sclerosis (ECTRIMS) held in Copenhagen. With over 50 invited talks and original oral and poster presentations, our researchers contributed to important discussions regarding the latest advancements in multiple sclerosis (MS) research, highlighting RC2NB's position as a center of scientific excellence.

Presentations by RC2NB experts focused on advanced neuroimaging techniques, computational methods for lesion classification, and novel biomarkers for tracking MS progression. Our researchers also shared insights on integrating deep learning and machine learning to improve diagnosis and disease monitoring, along with digital health solutions aimed at enhancing patient assessment and care.

Collaboration was a central theme at this year's ECTRIMS, with RC2NB's contributions underscoring the significance of translational research. Ongoing partnerships with international institutions are instrumental in refining treatment strategies and advancing patient-centered approaches.

In addition to the scientific discussions, ECTRIMS 2024 provided an opportunity to connect with researchers, clinicians, and industry partners. The exchange of ideas and expertise throughout the conference served as a reminder of our collective commitment to improving MS care.

Think group at ECTRIMS 2024.



SCIENTIFIC ADVISORY BOARD (SAB) RESEARCH MEETING 2024

In October 2024, RC2NB Hosted the Scientific Advisory Board (SAB) research meeting at the Biozentrum, University of Basel. This was an opportunity to reflect on a year of diverse research at RC2NB. The SAB commended the high productivity across all workstreams, highlighting a significant increase in joint publications as evidence of the collaborative and interdisciplinary nature of our research.

What distinguishes RC2NB is its uniquely integrated translational research environment. With well-defined patient cohorts, a robust clinical trial framework, and advanced tools for clinical phenotyping, our researchers effectively bridge the gap between laboratory findings and patient care. Cutting-edge neuroimaging, fluid biomarker analysis, and immunological monitoring further enhance our capacity to understand disease mechanisms and optimize treatments.

Scientific Advisory Board Research Meeting, October 2024



MS INFORMATION DAY 2024



MS INFORMATION DAY 2024, Özgür Yıldızlı's presentation.

On December 7, 2024 the MS Centre Basel (University Hospital Basel) and RC2NB hosted an event titled "Learning from Patient Care for Research and Therapy." This gathering focused on bridging the gap between clinical care and scientific research in multiple sclerosis (MS). Organized by Dr Johanna Oechtering, Prof Tobias Derfuss, and Prof Jens Kuhle, the event featured expert presentations and discussions on significant advancements in MS research and treatment. Key topics included the role of the Epstein-Barr virus (EBV) in MS pathogenesis, the potential of BTK inhibitors in addressing disease progression, and evidence-based strategies for managing affective disorders in MS. Attendees also received updates from the Swiss MS Society, learned about the benefits of hippotherapy for MS patients, and explored the future of personalized medicine, particularly within the Multiscript study.

A "Meet the Expert" session provided attendees with insights into various aspects of MS, including immunology, optical coherence tomography (OCT), pregnancy considerations, and ongoing clinical trials. The event concluded with a networking session, emphasizing the importance of collaboration among researchers, clinicians, and patients to advance MS research and care.



Tanja Stoll with a patient at the MS Information Day

MATTHIAS' STORY: LIVING AND THRIVING WITH MS

Multiple Sclerosis (MS) is a chameleon of a disease, changing its face daily, challenging you in unexpected ways, and ultimately teaching you more about yourself than you could have imagined. Matthias knows this all too well. His journey with MS is not just about a diagnosis; it's a story of resilience, humor, and the determination it takes to keep moving forward.

It all began in 1997 when, while crossing a street, his legs suddenly disappeared beneath him. Alarmed, he went to see his doctor, hoping to find out what had happened that day. Matthias was suspected of having MS with further check-ups to follow, leaving him still with some hope. Although he continued skiing, climbing, cycling, and even volunteering in the fire department's special unit, life wasn't like it used to be. "It wasn't the "maybe" diagnosis, but the look in my family's eyes that was the hardest part."

Looking back now, Matthias grins to his early attempts to outrun MS. "I tried to keep going like nothing had changed," he says, "but my body kept reminding me that it had." Slowly, his endurance weakened, and the once effortless activities began to demand more and more from him. By 2017, he gets increasingly dependent on the wheelchair, which became his new reality.

But here is the thing about Matthias: he doesn't let the wheelchair define him. "The chair is the easy part," he says with a smile. "It's the invisible challenges, such as spasticity, bladder issues, pain, and fatigue, that are the real battle." However, even on the hardest days, Matthias tries to keep his sense of humor. For Matthias, falling is not just a physical challenge; it's a metaphor for life. "Before I can get back up, I need a moment to re-coordinate my body. It's like a tipped-over fruit basket," he jokes. "Everything spills out, and it takes time to gather it all back."

Despite everything, Matthias continues to live boldly. One of his proudest moments was completing a 1.8 km Jogathon with the help of a robotic exoskeleton/Myosuit. "It took me three hours," he beams, "but I did it!"

For Matthias, staying active is about more than exercise, it's about feeling alive. A ride through nature on his recumbent bike can turn a tough day into something bearable. It's also his time of independence, a moment when he doesn't have to rely on anyone else. He can still ride on his own, and that freedom means everything. Monthly self-help group meetings provide not only a sense of community but also a sense of purpose. And while photography can be more challenging from a wheelchair, he refuses to give up on capturing the world from his unique perspective.

He finds hope in contributing to research through the Swiss MS Cohort and other RC2NB ongoing studies, believing, "If my experience can help someone else, why wouldn't I share it?" His advice to newly diagnosed patients is to seek support: "Don't face it alone. Talk to your doctor, join a self-help group, and connect with the MS Society. It's about building a team to face challenges together." Matthias sums up his journey with this: "Take it slow; I'm in a hurry." Every day is a challenge, but he pushes forward one step, one laugh, and one win at a time.



RALPH'S STORY: FROM A CHRISTMAS TRADITION TO A LIFE-CHANGING DIAGNOSIS

For many, the holiday season is filled with warmth, tradition, and moments to cherish. For Ralph, Christmas 2008 started just like that, a simple but meaningful ritual of hauling a freshly cut tree home on a sled. He never imagined that, within days, what seemed like routine muscle soreness would signal the start of an entirely new chapter in his life.

At first, he chalked up the discomfort to the physical effort of dragging the tree. But then, the sensation changed. A strange numbness crept up his right side, stretching from his foot to his chest. It was persistent, unusual, and concerning. Soon after, doctors gave him an unexpected diagnosis: multiple sclerosis (MS).

That winter was a turning point, but in the years since, Ralph has steadily adapted to life with MS. Over the years, his treatment has evolved, was less disruptive and helped controlling his disease, from self-administered injections every other day to daily tablets, and now, twice-yearly infusions. "In the beginning, injecting myself took a lot of willpower," he recalls. "And traveling for work with Interferon syringes? That was always an adventure at airport security." But despite the challenges, one thing has remained constant: his determination to stay active and independent (he came to our interview on his bike).

Though some symptoms linger, Ralph has found ways to adjust. Running for the bus or going for a jog may no longer be an option, but Nordic walking has become his go-to activity. His fingertips remain numb, but a simple habit, double-checking emails before sending them, keeps him on top of his work. From the outside, most people wouldn't even know he has MS unless he tells them.

Technology has also played a role in helping him navigate his condition. Ralph now uses dreaMS, a smart app designed for MS patients that tracks subtle changes in cognitive and physical abilities. His background in the chemical industry has given him a deep appreciation for data, so having a tool that provides real-time insights into his health makes perfect sense. But what truly motivates him is something far more personal, a close relative, who also has MS.

"I hope my participation in this study helps shape the future of MS care - not just for me, but for future generations and younger patients. I dream of more targeted, effective treatments, and with fewer side effects."

Looking back, Ralph remembers how overwhelming his diagnosis once felt. But knowledge, support, and time have reshaped his perspective. Today, MS is simply a part of his life, it influences his daily choices, but it doesn't define who he is. And through support of research and innovation, he hopes to play a small role in making life easier for future generations living with MS.



FINANCIAL STATEMENT

RC2NB ANNUAL REPORT 2024

FINANCIAL RESULTS AND RESEARCH IMPACT - 2024

In 2024, RC2NB used the funds available to advance our understanding of MS and related neuroimmunological disorders. We wish to thank our financial partners for their generous support that enables us to continue this pursuit.

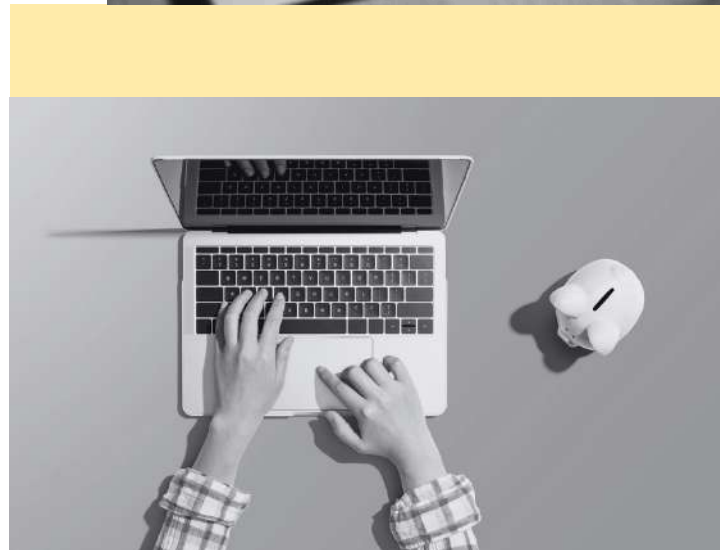
FINANCIAL OVERVIEW

Total operating income for the year amounted to CHF 3,561,408, a decrease from CHF 5,823,801 in 2023. This decrease is attributed to one-off contributions received in 2023 that were specifically intended to finance certain projects for the upcoming years, leading to an unusually high figure for that year. Additionally, a structural financial contribution to the institute was shifted from 2024 to 2025 which further explains the decrease. Income from other sources, however, was reasonably stable, reaching CHF 1,677,408 in 2024.

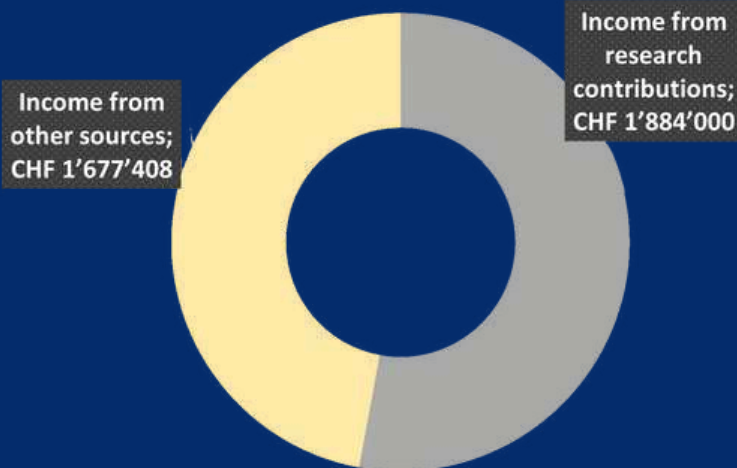
Expenses for the year totaled CHF 4,558,877, reflecting an increase from CHF 2,849,847 in 2023. This rise is attributed to expanded personnel costs and additional investments in consumable materials, laboratory services, and technical development to support ongoing and new research projects. Close to 90% of the total expenses are directly linked to the scientific output of RC2NB.

OUTLOOK

Moving forward, the focus remains on securing diversified funding sources and optimizing operational efficiency to continue advancing research in MS and related neuroimmunological disorders. We look forward to partnering with further stakeholders towards this goal.

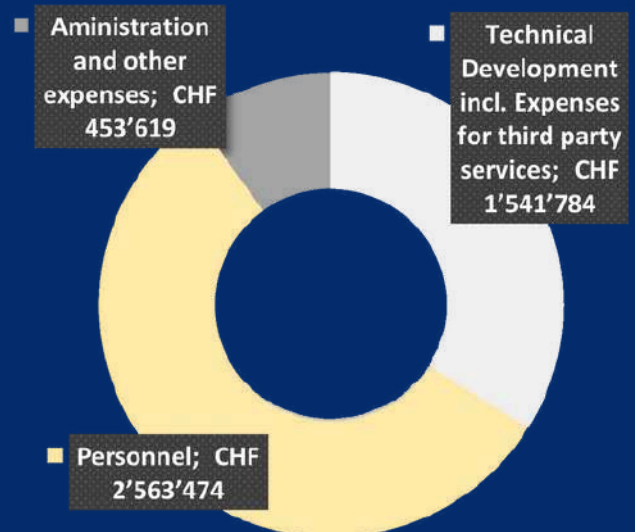


INCOME BY CATEGORY



TOTAL INCOME: 3 561 408 CHF

EXPENSES BY CATEGORY



TOTAL EXPENSES: 4 558 877 CHF

FINANCIAL STATEMENT 2024

	2024	2023
Income from research contributions	1 884 000 CHF	3 740 764 CHF
Income from other sources	1 677 408 CHF	2 083 037 CHF
Total Operating Income	3 561 408 CHF	5 823 801 CHF
Technical Development incl. expenses for third party services	-1 541 784 CHF	-873 268 CHF
Personnel	-2 563 474 CHF	-1 818 044 CHF
Administration and other expenses	-453 619 CHF	-158 535 CHF
Total Operating Expenses	-4 558 877 CHF	-2 849 847 CHF
Financial Income	30 999 CHF	1377 CHF
Financial Expenses	-2 855 CHF	679 CHF
Financial Result	28 145 CHF	698 CHF
Ordinary Result before allocation to restricted funds	-969 324 CHF	2 974 652 CHF
Assets allocated to restricted funds	294 318 CHF	-1 355 670 CHF
Ordinary Result after allocation to restricted funds	-675 006 CHF	1 618 982 CHF
Assets allocated to unrestricted funds	675 006 CHF	-1 618 982 CHF
Ordinary Result after allocation to unrestricted funds	0 CHF	0 CHF

EXPENSES BY COST CENTERS

RC2NB's Financial Statement 2024 was reviewed and approved by the auditor BDO AG. **Several projects of research groups in the RC2NB workstreams 2, 3 and 4 are currently funded independently and managed by the University Hospital or the University of Basel and therefore, not part of RC2NB's financial statement.**

	Personnel	Consumable and other lab services	Technical Development	Administration and other expenses	Total
Workstream 1	-783 022 CHF	-246 842 CHF	-898 020 CHF	-95 671 CHF	-2 023 555 CHF
Workstream 2	-1 277 560 CHF	-360 262 CHF	0 CHF	-152 502 CHF	-1 790 324 CHF
Workstream 3	-51 016 CHF	0 CHF	0 CHF	0 CHF	-51 016 CHF
Workstream 4	-43 928 CHF	0 CHF	0 CHF	-5 056 CHF	-48 984 CHF
Data Storage and Analysis	-145 892 CHF	-46 006 CHF	0 CHF	-5 236 CHF	-197 134 CHF
Management/Administration	-252 177 CHF	0 CHF	0 CHF	-175 215 CHF	-427 452 CHF
Research Funds	-9 879 CHF	0 CHF	0 CHF	-10 532 CHF	-20 412 CHF
Total	-2 563 474 CHF	-653 111 CHF	-898 020 CHF	-444 272 CHF	-4 558 877 CHF

EQUITY

	2024	2023
Equity as of 01.01	7 672 125 CHF	4 697 473 CHF
Income	3 589 553 CHF	5 824 499 CHF
Expenses	-4 558 877 CHF	-2 849 847 CHF
Equity as of 31.12	6 702 801 CHF	7 672 125 CHF

MAIN PARTNERING INSTITUTIONS AND RESEARCH SUPPORT

Thank you for supporting us in 2024!

We extend our heartfelt gratitude for the generous support and invaluable collaborations with institutional donors, foundations, and private individuals. These partnerships form the cornerstone of our research, driving our mission forward and amplifying our impact.



Our sponsors in Switzerland



Our Clinnova partners and locations around Europe

Basel (Switzerland)



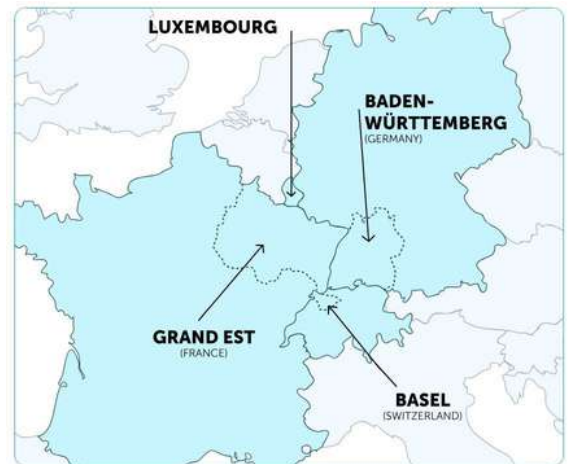
Grand Est (France)



Baden-Württemberg (Germany)



Luxembourg



Our dreAMS VS2 partners and locations around the world

- | | |
|-------------------|-----------------------|
| Austria Innsbruck | Italy Genova |
| Austria Graz | Italy Milano |
| Austria Wien | Italy Roma |
| Canada Toronto | Netherlands Amsterdam |
| Canada Vancouver | Norway Oslo |
| Germany Berlin | Spain Madrid |
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| Germany Dresden | USA San Francisco |
| Italy Bari | USA Boston |
| Italy Cagliari | |





RC2NB Administration team - Hanl L, Herrgott K, Limberg P, Suljakovic A.

MEMBERS AND AFFILIATES OF RC2NB

RC2NB ANNUAL REPORT 2024

ADMINISTRATION

- Kappos Ludwig, Prof (RC2NB CEO)*
- Granziera Cristina, Prof (RC2NB CO-CEO)*
- Limberg Philipp, MSc (RC2NB manager, project management dreaMS VS1 and dreaMS VS2)*

Cosandey Bebek, PhD (head of scientific communication & marketing)
Hanl Lea (CEO assistant and management assistant)

Herrgott Kathleen (scientific collab. and content creator)
Saupper Claudia, MSc (data architect)
Suljakovic Aida (admin. employee research)

DIGITAL FUTURE - WORKSTREAM 1

Group Members and Affiliates

dreaMS and digital biomarkers:

Granziera Cristina, Prof (research group leader)
Lorscheider Johannes, PD Dr (research group leader)
Hemkens Lars, Prof (PI VS2)
Müller Jannis, Dr, MSc (PI VS1)
Becherer Claudia, MAS (regulatory affairs)
Bezençon Thomas (master/medical student)
Cosandey Bebek, PhD (lead scientific project manager)
Haag Melanie, PhD (project management)
Hansen Dörthe (project management)
Kolb Sibylle (study nurse)
Lacalamita Melanie (study coordinator)

Limberg Marguerite (study nurse)
Lu Po-Jui (head of AI/industrial collaboration)
Mathes Vera, MSc (regulatory affairs)
Phavanh Vanny (study nurse)
Pless Silvan, MSc (neuropsychologist, PhD student)
Sala Rossella, MSc (study nurse)
Stoll Tanja, MSc (study nurse)
Vollmer Madeleine (Regulatory Affairs)
Wiencierz Andrea, PhD (statistician)
Wölfle Tim, Dr, MSc (clinician-scientist, PhD student)

Indivi Ltd: <https://indivi.io/>

Belachew Shibeshih, Dr
De Jong Corne
Dupont Guilhem
Reyes Oscar, PhD

Ella Gibbs
Adrian Garcia
(Healios/INDIVI; other employees of Healios (now INDIVI Ltd involved in dreaMS are not individually mentioned)

Neurostatus-UHB LtD

D'Souza Marcus, PD Dr (senior consultant/CEO)
Athanasopoulou Ioanna, PD Dr (neurologist)
Boos Lukas (assistant physician)
Brandt Jenny (Teaching Tools of the Medical Deanery)
Callegari Ilaria, Dr (neurologist)
Cerdá Fuertes Nuria Alicia, Dr (neurologist lead)
Corageoud Matthieu (IT)

Gysin Annalea (management assistant)
Heiniger Carla (management assistant)
Hug Gabriel (student/IT)
Kamm Christian, Prof (neurologist)
Kel Jakob (IT lead)
Lee Joanne (Sim Joo) (operations)

Demirtzoglou Anastasios (neurologist)
 Dinsenhacher Lisa, Dr (neurologist)
 Duhan Prerna (intern)
 Forman Barbara (operations & legal affairs)
 Fricker Evy (COO)
 Gamez Marcos (IT)
 Garcia Eddy (operations lead)
 Greselin Martina (PhD student)

Mallucci Giulia, Dr (neurologist)
 Minkova Lora (digital tools for HD & connection to the EHDN digital working group)
 Njuguna Steven (IT)
 Ryf Diego (master student)
 Tschirky Michelle (intern/IT)
 Trouillet Thomas (IT)
 Waiz Colleen (operations)

NOVEL IMAGING & FLUID BIOMARKERS - WORKSTREAM 2

Group Members and Affiliates

ThINK Basel

Prof Cristina Granziera team:

Granziera Cristina, Prof (RC2NB Co-CEO, senior consultant in neurology USB, research group leader)
 Aaisha Negeh Bah (student)
 Barker David Charles (student)
 Bar Zohar Noa (PhD student)
 Bosticardo Sara (PhD student)
 Cagol Alessandro, Dr (research fellow)
 Callegari Ilaria, Dr (research fellow)
 Chen Xinjie, Dr (PhD student)
 Dhital Bibek, Dr (research fellow)
 Galbusera Riccardo (PhD student)
 Gkotsoulas Dimitrios, Dr (research fellow)
 Greselin Martina (PhD student)
 Kaim Kornelius (student)
 Limberg Marguerite (research assistant)
 Lu Po-Jui, Dr (research fellow)
 Magnenat Victor (student)

Melie Garcia Lester, Dr (senior researcher)
 Meluso Marco (student)
 Müller Jannis, Dr, MSc (consultant in neurology USB, research group leader)
 Ocampo Pineda Mario Alberto, Dr (research fellow)
 Ruberte Esther, Dr (senior researcher)
 Sanabria Diaz Gretel, Dr (research fellow)
 Schädelin Sabine, MSc (statistician)
 Siebenborn Nina de Oliveira Soares (research fellow)
 Schönenberger Lukas (PhD student)
 Spagnolo Federico (PhD student)
 Suljakovic Aida (personal assistant)
 Weigel Matthias, Dr (senior researcher)
 Wenger Antonia (PhD student)
 Wölfle Tim (PhD student)

PD Athina Papadopoulou team:

Papadopoulou Athina, PD (senior consultant)
 Burget Villena Federico (doctoral student)
 Cerdá Fuertes Nuria Dr (post doc researcher)
 Ebner Katarina (doctoral student)
 Gugleta Alisa (master student)

Kuhlmann Jenni (doctoral student)
 Schönholzer Kean (PhD student)
 Sellathurai Shaumiya (doctoral student)

Prof Özgür Yaldizli team:

Yaldizli Özgür, Prof (research group leader, senior consultant)
 Aldea Andreea (assistant doctor)
 Müller Jannis (research fellow)

Tan Gizem (master student)
 Weisse Heloise (master student)

Prof Regina Schläger team:

Schläger Regina, Prof (research group leader, senior consultant)
 Bohnert Nicola (administration)
 Kesenheimer Eva Dr (PhD student)
 Konjevod Valentina (scientific assistant, doctoral student)

Penker Simone (scientific assistant, doctoral student)
 Sander Laura Dr (post doc)
 Wendebourg Janina Dr med (post doc)

PD Katrin Parmar team:

Parmar Katrin (senior consultant at the Reha Rheinfelden)
 Charidimos Tsagkas, PhD (research fellow, Currently post doc at NIH, Bethesda,US)

Prof Jens Kuhle team:

Swiss MS Cohort Study and Clinical Neuroimmunology - Fluid Biomarker Laboratory

Kuhle Jens, Prof (head of the multiple sclerosis centre and neuroimmunology unit, senior consultant)
 Benkert Pascal, Dr (head of SMSC datacentre, senior statistician)
 Billot Ghislaine (study nurse)

Miteva Suzana (study nurse)
 Oechtering Johanna, Dr (senior neurologist/postdoc)
 Orleth Annette, Dr (post doc)
 Phavanh Vanny (study nurse)
 Rhyner Miriam (study nurse)



Brunner Caroline (study nurse)
 Demuth Lilian (study coordinator)
 Einsiedler Maximilian (senior neurologist/post-doc)
 Gomez Juan Vilchez (research technician)
 Gress Ulrich (study coordinator)
 Hofer Lisa (statistician)
 Lacalamita Melanie (study coordinator)
 Leppert David, Prof (senior research associate)
 Limberg Marguerite (study nurse)
 Maleska Maceski Aleksandra Maleska, MSc (bioengineer)

Rodriguez Calvo Mauricio (study coordinator)
 Salfati Jonathan (data manager)
 Schaedelin Sabine, MSc (statistician)
 Schmid Genevieve (study nurse)
 Stanojevic Daniela (study nurse)
 Subramaniam Suvitha, MSc (data scientist)
 Willemse Eline, Dr (post doc)
 Zadic Amar (research technician)

INTERNATIONAL CLINNOVA CONSORTIUM

Clinnova Basel

Granziera Cristina, Prof (principal investigator)
 Cosandey Bebekka, PhD (lead scientific project manager)
 Stoll Tanja, MSc (study nurse)

UNDERSTANDING THE IMMUNE SYSTEM - WORKSTREAM 3

Group Members and Affiliates

Prof Tobias Derfuss Team:

Derfuss Tobias, Prof (senior consultant, vice chair of the department of neurology, head neurology outpatient Clinic)
 Billot Ghislaine (study nurse)
 Brunner Caroline (study nurse)
 Galli Edoardo Dr (post doc)
 Hong Chang (undergraduate student)
 Lacalamita Melanie (study coordinator)
 Nadišauskaitė Rūta (PhD student)

Miteva Suzana (study nurse)
 Phavanh Vanny (study nurse)
 Raach Yakine (PhD student)
 Rhyner Miriam (study nurse)
 Sakiri Elif (PhD student)
 Sanderson Nicholas, PD, PhD, (senior scientist)
 Schneider Mika (PhD student)

Prof Matthias Mehling team:

Mehling Matthias, Prof (senior consultant)
 Boog Olivier (PhD student)
 Coray Mali (MD-PhD student)

Epple Varenka, Dr (research associate)
 Fuhrmann Jakob, Dr (research associate)

Prof Anne-Katrin Pröbstel team:

Pröbstel Anne-Katrin, Prof (senior consultant)
 Berve Kristina (post doc)
 Beyerle Miriam (MD doctoral student)
 Cullen Pauline (scientific coordinator)
 Dürrenberger Tim (doctoral student)
 Flammer Julia (resident/post doc)
 Gomes Ana (PhD student)
 Gutzwiller Julia (clinical study coordinator)
 Gutzwiller Sophia (student assistant)
 Häfelfinger Marco (master student)
 Kulsvehagen Laila (PhD student)
 Lecourt Anne-Cathérine (lab manager/technician)

Lerner Jasmine (master student)
 Lipps Patrick (MD doctoral student)
 Lutz Luc (master student)
 Neziraj Tradite, Dr (resident/post doc)
 Otto Maximilian (undergraduate student)
 Pössnecker Elisabeth (PhD student)
 Pretzsch Roxanne (resident/post doc)
 Scherhag Florine (master student)
 Siewert Lena, Dr (post doc)
 Wettig Angéline (master student)
 Wetzel Nora (MD-PhD student)

PRAGMATIC EVIDENCE - WORKSTREAM 4

Group Members and Affiliates

Prof Lars Hemkens, Pragmatic Evidence Lab:

Hemkens Lars, Prof (research group leader; senior scientist)
 Axfors Cathrine, Dr (scientific coordinator, research fellow)
 Beer Maximilian (master student medicine)
 Chaboud Louise (PhD student clinical research)
 Düblin Pascal (application developer)
 Hansen Sina (senior project manager)
 Hirt Julian, Dr (research fellow)

Janiaud Perrine, Dr (head of Pragmatic Data Science Center, research fellow)
 Macias Alonso Ana Karen (master student bioengineering)
 Mohamadi Marjan (master student epidemiology)
 Sison Ada (master student epidemiology)
 Andreas Schmitt, MD (research fellow)



AWARDS, DISTINCTIONS AND OTHER ACHIEVEMENTS IN 2024

Aldea Andreea-Alexandra – Awarded the Young Talent in Clinical Research scholarship by the Swiss Academy of Medical Sciences.

Cagol Alessandro – Recipient of the 2024 ISMRM Magna Cum Laude Merit Award.

Chen Xinjie – Received an ISMRM 2024 travel stipend and was selected for a Power Pitch for the abstract, “Age-Impacted Cortical Regions Demonstrate Associations with Clinical Relevance in Multiple Sclerosis.” Also awarded an ECTRIMS travel grant for research on normative trajectories of R1, R2*, and susceptibility values in the healthy human brain cortex.

Giacomelli Elisabetta – Best Master’s Thesis 2024 award during the Department of Biomedical Engineering Research Day for her thesis, “Identification of 9.4T MRI Sequences for Enhanced Cellular Visualization of Multiple Sclerosis Lesions.”

Greselin Martina – Awarded the Trainee (Educational) Stipend from ISMRM for her abstract, “Gadolinium Contrast-Enhanced Lesion Segmentation in Multiple Sclerosis: A Deep-Learning Approach.”

Kappos Ludwig – Otto Hommes Memorial European Charcot Foundation distinguished lecture at the 2024 Annual ECF Symposium

Kuhle Jens – Received the very prestigious 2024 Sobek Research Prize.

Kuhle Jens – Received the Best Scientific Achievement Award from Neurology USB for the publication on “Serum Glial Fibrillary Acidic Protein and Neurofilament Light Chain Levels Under B-Cell Depleting Treatment in MS” (see publication nr 9 on p 37).

Kuhle Jens and Kappos Ludwig – Recognized as Highly Cited Researchers (Clarivate) in the year 2024.

Kuhlmann Jenni – 1st Poster Prize at the Day of Clinical Research 2024 (DKF) for her study on music therapy in multiple sclerosis.

Lipps Patrick – 2nd place in the YouClin Thesis Award 2024 (August 2024).

Müller Jannis – Received the Return Grant-Pool für Innere Medizin from the University Hospital Basel, and the SNF Mobility Return-Grant from the Swiss National Science Foundation (SNSF).

Pretsch Roxanne – Received for her MD thesis, “The Role of Regulatory B Cell Properties in Multiple Sclerosis – Future Therapeutic Implications,” the Hertie-Stiftung Award.

Spagnolo Federico – Awarded stipends from ECTRIMS 2024 and ISMRM 2024, along with a travel grant for the MRI Workshop in Paris. Achieved third place in the ICPR 2024 MS Lesion Segmentation Competition.

Wetzel Nora – Received a 2024 SNF Mobility Grant.

Wölfle Tim – Awarded the SNS 2024 Déjérine-Dubois Prize – Best Free oral presentation in Clinical Research for his work, “Classification of MS Severity Subgroups Using Smartphone-Based Motor Tests and Machine Learning”.

Yaldizli Özgür – Received, as part of an international collaboration, an ERA-NET NEURON grant to study the significance of the choroid plexus in multiple sclerosis and chronic pain.

COMPLETED PHD, DOCTORAL THESES AND MASTER THESES

Completed PhDs

Chen Xinjie, PhD (Department of Biomedical Engineering)
Galbusera Riccardo, PhD (Department of Biomedical Engineering)
Holdermann Sebastian, PhD (Department of Biomedicine)
Kulsvehagen Laila, PhD (Department of Biomedicine)

Completed Medical Theses

Berati Kristel, Doctoral Thesis (Medical Faculty Basel)
Stössel Marc, Doctoral Thesis (Medical Faculty Basel)

Completed Masters

Alonso Ana Karen Macias, MD (Biomedical Engineering; University of Lübeck, Germany)
Ba Aisha Negeh, MD (Department of Biomedical Engineering)
Chaboud Louise, MD (Comparative Effectiveness Research; Université Paris Cité, France)
Jayakumar Tejeswini, MD (Department of Biomedical Engineering)
Müller Jannis, Master of Science (MSc) in Clinical Research at Dresden International University (Germany) and Harvard T.H. Chan School of Public Health (USA).

PUBLICATIONS IN PEER REVIEWED JOURNALS

Highlighted papers are displayed in red

Authors displayed in bold are members of RC2NB working groups

1. Abdelhak A, Antweiler K, Kowarik MC, Senel M, Havla J, Zettl UK, Kleiter I, Skripuletz T, Haarmann A, Stahmann A, HussA, Gingele S, Krumbholz M, **Benkert P, Kuhle J**, FriedeT, Ludolph AC, Ziemann U, Kümpfel T, Tumani H. Serum glial fibrillary acidic protein and disability progression in progressive multiple sclerosis. *Ann Clin Transl Neurol.* 11(2):477-85.
2. Ahmad S, Imtiaz MA, Mishra A, Wang R, Herrera-Rivero M, Bis JC, Fornage M, Roshchupkin G, Hofer E, Logue M, Longstreth WT, Xia R, Bouteloup V, Mosley T, Launer LJ, Khalil M, **Kuhle J**, Rissman RA, Chene G, Dufouil C, Djoussé L, Lyons MJ, Mukamal KJ, Kremen WS, Franz CE, Schmidt R, Debette S, Breteler MMB, Berger K, Yang Q, Seshadri S, Aziz NA, Ghanbari M, Ikram MA. Genome-wide association study meta-analysis of neurofilament light (NfL) levels in blood reveals novel loci related to neurodegeneration. *Commun Biol.* 9;7(1):1103.
3. Amstutz A, Schönenberger CM, Speich B, Griessbach A, Schwenke JM, Glasstetter J, James S, Verkooijen HM, Nickolls B, Relton C, **Hemkens L**, Chammartin F, Gerber F, Labhardt ND, Schandelmaier S, Briel M. Characteristics, consent patterns, and challenges of randomized trials using the Trials within Cohorts (TriWiCs) design - A scoping review. *J Clin Epidemiol.* 174:111469.
4. Androdias G, Lünemann JD, Maillart E, Amato MP, Audoin B, Bruijstens AL, Bsteh G, Butzkueven H, Ciccarelli O, Cobo-Calvo A, **Derfuss T**, Di Pauli F, Edan G, Enzinger C, Geraldes R, Granziera C, Hacoheh Y, Hartung HP, Hynes S, Inglese M, **Kappos L**, Kuusisto H, Langer-Gould A, Magyari M, Marignier R, Montalban X, Mycko MP, Nourbakhsh B, Oh J, Oreja-Guevara C, Piehl F, Prosperini L, Sastre-Garriga J, Sellebjerg F, Selmaj K, Siva A, Tallantyre E, van Pesch V, Vukusic S, Weinstock-Guttman B, Zipp F, Tintoré M, Iacobaeus E, Stankoff B. De-escalating and discontinuing disease-modifying therapies in multiple sclerosis. *Brain.* 2024:awae409.
5. Arnett S, Chew SH, Leitner U, Hor JY, Paul F, Yeaman MR, Levy M, Weinshenker BG, Banwell BL, Fujihara K, Abboud H, Dujmovic Basuroski I, Arrambide G, Neubrand VE, Quan C, Melamed E, Palace J, Sun J, Asgari N, Broadley SA, Guthy Jackson International Consortium*. Sex ratio and age of onset in AQP4 antibody-associated NMOSD: a review and meta-analysis. *J Neurol.* 271(8):4794-812 (**A-K Pröbstel, member of Guthy Jackson International Clinical Consortium**).
6. **Axfors C**, Schmitt AM, **Janiaud P**, Van'tHooft J, Abd-Elsalam S, Abdo EF, Abella BS, Akram J, Amaravadi RK, Angus DC, Arabi YM, Azhar S, Baden LR, Baker AW, Belkhir L, Benfield T, Berrevoets MAH, Chen CP, Chen TC, Cheng SH, ChengCY, Chung WS, Cohen YZ, Cowan LN, Dalgard O, de AlmeidaE Val FF, de LacerdaMVG, de Melo GC, Derdel, Dube V, ElfakirA, Gordon AC, Hernandez-Cardenas CM, Hills T, Hoepelman AIM, Huang YW, Igau B, Jin R, Jurado-Camacho F, Khan KS, KreamsnerPG, Kreuels B, Kuo CY, Le T, Lin YC, Lin WP, Lin TH, Lyngbakken MN, McArthur C, McVerry BJ, Meza-Meneses P, Monteiro WM, Morpeth SC, Mourad A, Mulligan MJ, Murthy S, Naggie S, Narayanasamy S, Nichol A, Novack LA, O'Brien SM, Okeke NL, Perez L, Perez-Padilla R, Perrin L, Remigio-Luna A, Rivera-Martinez NE, Rockhold FW, Rodriguez-Llamazares S, Rolfe R, Rosa R, Røsjø H, Sampaio VS, Seto TB, Shahzad M, Soliman S, Stout JE, Thirion-Romero I, Troxel AB, Tseng TY, Turner NA, Ulrich RJ, Walsh SR, Webb SA, Weehuizen JM, Velinova M, Wong HL, Wrenn R, ZampieriFG, Zhong W, Moher D, Goodman SN, Ioannidis JPA, **Hemkens L**. Author Correction: Mortality outcomes with hydroxychloroquine and chloroquine in COVID-19 from an international collaborative meta-analysis of randomized trials. *Nat Commun.* 15(1):1075.
7. Barakovic M, **Weigel M, Cagol A, Schaedelin S, Galbusera R, Lu PJ, Chen X, Melie-Garcia L, Ocampo-Pineda M**, Bahn E, Stadelmann C, Palombo M, **Kappos L, Kuhle J**, Magon S, **Granziera C**. A novel imaging marker of cortical « cellularity » in multiple sclerosis patients. *Sci Rep.* 14(1):9848.
8. Becher B, **Derfuss T**, Liblau R. Targeting cytokine networks in neuroinflammatory diseases. *Nat Rev Drug Discov.* 23(11):862-79.
9. **Benkert P, Maleska Maceski A, Schaedelin S, Oechtering J, Zadic A, Vilchez Gomez JF, Melie-Garcia L, Cagol A, Galbusera R, Subramaniam S, Lorscheider J, Galli E, Mueller J, Fischer-Barnicol B**, Achtnichts L, Findling O, Lalive PH, Bridel C, Uginet M, Müller S, Pot C, Mathias A, Du PasquierR, Salmen A, Hoepner R, Chan A, Disanto G, Zecca C, **D'Souza M, Hemkens L, Yaldizli Ö, Derfuss T**, Roth P, Gobbi C, Brassat D, Tackenberg B, Pedotti R, Raposo C, Oksenberg J, Wiendl H, Berger K, Hermesdorf M, Piehl F, Conen D, Buser A, **Kappos L, KhalilM, Granziera C, Abdelhak A, Leppert D, Willemsse E, Kuhle J**, Swiss MS Cohort study (SMSC). Serum Glial Fibrillary Acidic Protein and Neurofilament Light Chain Levels Reflect Different Mechanisms of Disease Progression under B-Cell Depleting Treatment in Multiple Sclerosis. *Ann Neurol.* 97(1):104-15.

10. Blant JC, De Rossi NN, Gold R, Maurousset A, Kraemer M, Romero-Pinel L, Misu T, Ouallet JC, Pallix Guyot M, Gerevini S, Bakirtzis C, Piñar Morales R, Vlad B, Karypidis P, Moisset X, **Derfuss T**, Jelcic I, Martin-Blondel G, Ayzenberg I, McGraw C, Laplaud DA, Du Pasquier RA, Bernard-Valnet R, for CORPUS and Italianstudy groups. Presentation and Outcome in SIP-RM and Natalizumab-Associated Progressive Multifocal Leukoencephalopathy: A Multicenter Cohort Study. *Neurol Neuroimmunol Neuroinflamm*. 11(5):e200281.
11. Boesen K, **Hemkens L, Janiaud P, Hirt J**. Publicly available continuously updated topic specific databases of randomised clinical trials: A scoping review. medRxiv. 2024.11.18.24317477.
12. **Bosticardo S**, Schiavi S, **Schaedelin S**, Battocchio M, Barakovic M, **Lu PJ, Weigel M, Melie-Garcia L, Granziera C**, Daducci A. Evaluation of tractography-based myelin-weighted connectivity across the lifespan. *Front Neurosci*. 17:1228952.
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