Abstract Book

2022 VIRTUAL edition

MS State of the Art

Symposium 2022

MS Swiss Multiple Sclerosis Society

MS State of the Art Symposium

«New Frontiers in MS – Therapy across the Age Span»

Dear Colleagues,

It is with great pleasure that we invite you to this year's 24th MS State of the Art Symposium, organized by the Swiss MS Society and its Medico Scientific Advisory Board.

This symposium is dedicated to discussing **«New Frontiers in MS – Therapy across the Age Span»**. It will shed light on the very young persons with Multiple Sclerosis (MS), and the elderly patients alike. Treatment recommendations require a thorough consideration of the individual factors determining the course of MS in these patient groups.

In the plenary morning sessions, five national and international experts will share their expertise on this theme. **Brenda Banwell (USA)** will give speech on pediatric MS, while **Thomas Berger (AT)** will elaborate on the topic of immunosenescence. **Ilijas Jelcic and Roland Martin** will discuss their findings after the first years of practicing stem cell transplantation in their clinic. Immunotherapy treatment options continue to emerge rapidly, and **Andrew Chan** will give an overview and outlook on the near future.

The afternoon session, with two sets of parallel workshops, will address specific topics relevant to daily practice, and encourage you to ask your own questions and engage in the discussion. In Workshop A the speakers will give an introduction to evidence-based **Complementary Medicine**. Workshop B is dedicated to **Nutrition and Microbiome**. Covid-19 continues to have a huge impact on our daily lives. Hence the final workshop **Covid-19 – What we know Today** is offered parallel in German, French and Italian.

In the name of the organisers and speakers, we hope that the programme meets your interest, and are looking forward to meeting you in Lucerne.

PD Dr. med. Sandra Bigi
Head of the Programme Committee,
And Member of the Steering Committee
of the Medico Scientific Advisory Board

Patricia Monin
Swiss MS Society
Director

Welcome from the Swiss Neurological Society

Dear Colleagues,

On behalf of the Swiss Neurological Society (SNS) it is a great pleasure to welcome you to the 24th MS State of the Art Symposium!

Multiple Sclerosis (MS) is a very important topic for the entire Swiss Neurology, involving many colleagues in hospitals and private practices. The development of effective and destiny changing treatments for MS patients in the last 30 years, including a steadily growing number of medicaments and the possibility of autologous stem cell transplantation, is an impressive example for the overwhelming diagnostic and therapeutic progress in neurology.

We are very proud to announce that the SNS and the Swiss MS Society decided to enter a formalized partnership. The aim of the SNS is to support the important activities of the Swiss MS Society in respect to an optimized patient care, the medical specialist training, and the continuing education. We already initialized first common actions such as to formulate a joint opinion in the Corona pandemic and we are ready to support the future important activities of the Swiss MS Society.

The topic of the symposium «New Frontiers in MS – Therapy across the Age Span» is of high importance for neurologists treating MS patients, and the different national and international speakers cover all aspects important for neurologists in hospitals and private practices. I wish you a very interesting, enjoyable meeting!

Prof. Dr. med. Hans H. Jung
Swiss Neurological Society
Past President

General Information

Date

Saturday, January 29, 2022, 10.15 – 15.15

Venue

Virtual edition

Programme Committee

Sandra Bigi, Bern
Adam Czaplinski, Zurich
Britta Engelhardt, Bern
Caroline Pot, Lausanne

Organisation

Swiss Multiple Sclerosis Society and its Medico Scientific Advisory Board

Contact

Swiss Multiple Sclerosis Society
Josefstrasse 129, CH-8031 Zurich
symposium@multiplesklerose.ch

Credits

The Swiss Neurological Society awards 5.0 credit points.

www.ms-state-of-the-art.ch
symposium@multiplesklerose.ch

Contacts

Programme Committee and Chairpersons

Sandra Bigi, Bern
– University Hospital Bern, Inselspital
Department of Neurology and
Department of Pediatrics
– University of Bern
Institute of Social and Preventive Medicine

Adam Czaplinski, Zurich
– Bellevue Medical Group
– Clinic for Neurology Hirslanden

Britta Engelhardt, Bern
University of Bern
Theodor Kocher Institute

Caroline Pot, Lausanne
Lausanne University Hospital (CHUV)
Service of Neurology

Welcome Speech

Hans Jung, Zurich
Swiss Neurological Society
Past-President

Christoph Lotter, Zurich
Swiss Multiple Sclerosis Society
Co-Director

Speakers (Lectures)

Brenda Banwell, Philadelphia (USA)
Children's Hospital of Philadelphia
Division of Neurology

Thomas Berger, Vienna (AT)
Medical University of Vienna
Department of Neurology

Andrew Chan, Bern
University Hospital Bern, Inselspital
Department of Neurology

Ilijas Jelcic, Zurich
University Hospital Zurich
Neurology Clinic

Roland Martin, Zurich
University Hospital Zurich
Neurology Clinic

Speakers (Workshops)

Tobias Derfuss, Basel
University Hospital Basel
Neurologic Clinic and Policlinic

Lara Diem, Bern
University Hospital Bern, Inselspital
Department of Neurology

Renaud Du Pasquier, Lausanne
Lausanne University Hospital (CHUV)
Service of Neurology

Giuseppe Locatelli, Bern
University of Bern
Theodor Kocher Institute

Oriol Manuel, Lausanne
Lausanne University Hospital (CHUV)
Infectious Diseases Service

Anne-Katrin Pröbstel, Basel
– University Hospital Basel
Neurologic Clinic and Policlinic
– University Hospital and University of Basel
Research Center for Clinical
Neuroimmunology and Neuroscience (RC2NB)

Anke Salmen, Bern
University Hospital Bern, Inselspital
Department of Neurology

Mireia Sospedra, Zurich
University of Zurich
Neuroimmunology and Multiple Sclerosis
Research

Claudia Witt, Zurich
University Hospital Zurich
Institute for Complementary and
Integrative Medicine

Ursula Wolf, Bern
University of Bern
Institute of Complementary and
Integrative Medicine

MS Researcher Poster Presentations

Maud Bagnoud, Bern

University Hospital Bern, Inselspital
Department of Neurology

Sandra Bigi, Bern

– University Hospital Bern, Inselspital
Department of Neurology and
Department of Pediatrics
– University of Bern
Institute of Social and Preventive Medicine

Jonas Bossart, Zurich

University of Zurich
Epidemiology, Biostatistics & Prevention
Institute

Mohamed Bouri, Lausanne

– Lausanne University Hospital (CHUV)
MySpace laboratory
– EPFL Lausanne
REHAssist

Donatella De Feo, Zurich

University of Zürich
Institute of Experimental Immunology

Samuel Jones, Lausanne

– Lausanne University Hospital (CHUV)
Laboratory of Neuroimmunology
– Lausanne University Hospital (CHUV)
Service of Neurology

Vasileia Kalaitzaki, Zurich

– University Hospital Zurich
Neuroimmunology and
Multiple Sclerosis Research
– University of Zurich
Institute of Laboratory Animal Science

Antonios Katsoulas, Zurich

University of Zurich
Institute of Laboratory Animal Science

Myrta Kohler, St. Gallen

– Eastern Switzerland University
of Applied Sciences
Institute of Applied Nursing Science
– Clinics of Valens
Rehabilitation Centre Valens

Zina-Mary Manjaly, Zurich

– Schulthess Clinic, Zurich
Department of Neurology
– ETH Zurich
Department of Health Sciences and Technology

Amandine Mathias, Lausanne

– University of Lausanne
Laboratory of Neuroimmunology
– Lausanne University Hospital (CHUV)
Service of Neurology

Johanna Oechtering, Basel

– University Hospital Basel
Neurologic Clinic and Policlinic
– University Hospital and University of Basel
Research Center for Clinical Neuroimmunology
and Neuroscience (RC2NB)

Amalric Ortlieb, Lausanne

– Lausanne University Hospital (CHUV)
MySpace laboratory
– EPFL Lausanne
REHAssist

continues
on next page

Nadine Patt, Valens
Clinics of Valens
Rehabilitation Centre Valens

Ines Pereira, Zurich
University of Zurich & ETH Zurich
Translational Neuromodeling Unit

Maximilian Pistor, Bern
University Hospital Bern, Inselspital
Department of Neurology

Jana Remlinger, Bern
University Hospital Bern, Inselspital
Department of Neurology

Mina Stanikic, Zurich
– University of Zurich
Epidemiology, Biostatistics & Prevention Institute
– University of Zurich
Institute for Implementation Science in Health Care

Solenne Vigne, Lausanne
– Lausanne University Hospital (CHUV)
Laboratory of Neuroimmunology
– Lausanne University Hospital (CHUV)
Service of Neurology

Verena Witzig Brändli, St. Gallen
Eastern Switzerland University of Applied Sciences Institute of Applied Nursing Science

Donate now with TWINT!

Scan the QR code with the TWINT app

Confirm amount and donation

Swiss MS Society:
We care for persons with MS

MS Swiss Multiple Sclerosis Society

«New Frontiers in MS – Therapy across the Age Span»

Session 1	**Chairpersons:** Adam Czaplinski, Zurich Britta Engelhardt, Bern
10.15 – 10.30	Christoph Lotter, Zurich & Hans Jung, Zurich **Welcome from the Swiss MS Society & the Swiss Neurological Society**
10.30 – 11.00	Ilijas Jelcic & Roland Martin, Zurich **Stem Cell Transplantation in MS – What we have learned from Practice**
11.00 – 11.30	Andrew Chan, Bern **Multiple Sclerosis 2022 – How many more Therapies do we need?**
11.30 – 11.45	Coffee Break
Session 2	**Chairpersons:** Sandra Bigi, Bern Caroline Pot, Lausanne
11.45 – 12.15	Brenda Banwell, Philadelphia (USA) **Pediatric MS – Current Treatment Strategies and Future Directions**
12.15 – 12.45	Thomas Berger, Vienna (AT) **MS in the Elderly – Immunosenescence and Implications for Management**
12.45 – 13.30	Lunch Break

Ilijas Jelcic

«I am a senior physician at the Neuroimmunology and MS Research Section (nims), University Hospital Zurich, and head the Neuroimmunology outpatient clinic, the neurological day clinic, the aHSCT-in-MS service and the cerebrospinal fluid (CSF) laboratory of the Department of Neurology. My main research interests are autologous hematopoietic stem cell transplantation for the treatment of multiple sclerosis, cerebrospinal fluid diagnostics in multiple sclerosis and other neuroimmunological disorders, as well as diagnostic and therapeutical approaches in JC virus-caused progressive multifocal leukoencephalopathy (PML) and other neuroinfectious diseases.»

Roland Martin

«I am a full professor for neurology and neuroimmunology at the University Zürich and head the Neuroimmunology and Multiple Sclerosis Research Section and MS outpatient clinic at the University Hospital Zurich. The main interests of my group are disease mechanisms of MS, cellular immunology, disease mechanisms of JC polyoma virus-mediated progressive multifocal leukoencephalopathy (PML) and developing novel treatments for MS and PML besides providing care for MS patients in one of the largest MS centers in Switzerland. I have received several awards, published over 400 scientific articles and filed numerous patents in the above areas. My group and I developed more than 10 projects from idea to early clinical proof-of-concept trials.»

Ilijas Jelcic & Roland Martin, Zurich

Stem Cell Transplantation in MS

What we have learned from Practice

Autologous hematopoietic stem cell transplantation (aHSCT) has been used for the treatment of highly active relapsing-remitting or progressive multiple sclerosis (MS) since 1995. Based on strong data regarding efficacy and improved safety of aHSCT in MS, the Swiss Federal Office of Public Health (FOPH) granted approval in June 2018 with the requirement that patients participate in a prospective registry («aHSCT-in-MS»). We here present the first safety and efficacy data for aHSCT-in-MS in Switzerland and summarize what we have learned from practice.

MS patients received aHSCT according to the BEAM-ATG protocol, because they had experienced inflammatory breakthrough activity and/or progression of MS despite highly effective disease-modifying therapy (DMT). We prospectively monitored adverse events (AE) and efficacy outcomes such as «no evidence of disease activity (NEDA)», i.e. absence of relapses, new or contrast-enhancing MRI lesions and clinical

progression, defined as sustained progressive worsening of expanded disability status scale (EDSS). Safety was analyzed in the first 35 patients, and efficacy in 27 patients, who had >12 months of follow-up.

At baseline, median age was 40 years (range 25-54), median disease duration 9.1 years (range 1.6-19.7) and median EDSS 4.0 (1.5-6.5). 16 (45.7%) patients had relapsing-remitting MS, 19 (54.3%) progressive MS. Failure of approved DMT before aHSCT included ocrelizumab (11), rituximab (11), fingolimod (11) and natalizumab (4). Median post-aHSCT follow-up was 23 months (range 6-61). Most patients developed mucotoxic and infectious AE, most frequently mucositis and/or enteritis (82.9%) and usually in the first 20 days post-aHSCT. Serious AE occurred in 22/35 patients with consecutive good recovery. 2 patients with secondary progressive MS committed assisted suicide 19 and 23 months post-aHSCT because of subjective perception of progression, although NEDA was confirmed in both cases. NEDA status was achieved in 22/27 (84.5%) patients at last follow-up. Until last follow-up, we observed sustained EDSS improvement in 20/35 (57.1%) patients, stable EDSS in 9/25 (25.7%) and EDSS-relevant progression in 6/35 (17.1%) patients.
In conclusion, safety of aHSCT-in-MS is acceptable, and efficacy outcomes are similar to other aHSCT studies and better than approved DMT. However, aHSCT-in-MS requires thorough psychiatric screening and follow-up, vigilant monitoring especially regarding infectious AE and antimicrobial prophylaxis.

Ilijas Jelcic & Roland Martin
University Hospital Zurich
Department of Neurology
Neuroimmunology and Multiple Sclerosis Research Section

Notes

Andrew Chan

«I am Head of the Medical Division Neuro, Inselspital, University Hospital of Bern. After studying medicine and obtaining a doctorate at the University of Hamburg, I completed my specialist training at the University of Würzburg and continued my professional development as Senior Physician at the Universities of Göttingen and Bochum. I have published widely in the field of MS, including papers on molecular markers of disease progression and risk of immunotherapy, treatment optimization and patient monitoring. I have been the principal investigator for several clinical studies in MS. I have also been involved in the development of national treatment guidelines.»

Multiple Sclerosis 2022 – How many more Therapies do we need?

The MS-treatment armamentarium is constantly growing. In comparison to existing medications some of the new additions harbor similar presumed mechanisms of action (e.g. sphingosin-1 phosphate receptor modulators ozanimod, Zeposia®; siponimod, Mayzent®; anti CD20 monoclonal antibody ofatumumab, Kesimpta®). Other new approvals involve different application forms (subcutaneous natalizumab, Tysabri s.c.™) or a substance (diroximelfumarate, Vumerity®) with bioequivalence of the active metabolite of dimethylfumarate (Tecfidera®).

Despite seeming similarities, specific pharmacodynamic (e.g. partial agonistic/antagonistic effects, epitope binding) and pharmacokinetic aspects (e.g. metabolites) may govern differential biological effects. Ideally, new treatments should assist with current unmet medical needs, e.g. treatment of vulnerable populations such as elderly pwMS, or during the ongoing Covid-19 pandemia. In this context, evolving data underscore the role also of «older» substances. Given the relative lack of prognostic, individualizing biomarkers, practicing neurologists still rely on relatively stereotypic procedures as reflected in respective guidelines. The Medico Scientific Advisory Board of the Swiss MS Society will update its last treatment recommendation from 2019 in early 2022 and also focus on specific situations (e.g. pregnancy).

Andrew Chan
University Hospital Bern, Inselspital
Department of Neurology

Brenda Banwell

«I am the Chief of Neurology and Director of the Neuroscience Center at CHOP and Professor of Neurology and Pediatrics, University of Pennsylvania. I serve as the Co-Director of the Neuroimmune program. Internationally, I am the Chair of the International Pediatric Multiple Sclerosis Study Group as well as the Medical and Scientific Advisory Board of the Multiple Sclerosis International Federation.»

Pediatric MS – Current Treatment Strategies and Future Directions

The diagnosis of multiple sclerosis (MS) in children and adolscents has been aided by the inclusion of pediatric patients in the formal McDonald criteria. The suitability of these criteria have been shown to be sensitive and specific in the pediatric MS context. Diagnoses to consider in the differential will be reivewed, as the diagnosis of MS requires exclusion of alternative diagnoses. In particular, consideration of MOG-associated demyelination (MOGAD) has emerged as an important diagnosis to consider, especially in children younger than 11 years. Clinical and MRI features of MS and MOGAD will be contrasted.

Treatment of pediatric-onset MS is evolving with the increasing recognition of the importance of early initiation of highly effective therapy and with ongoing formal clinical trials. Current and future therapeutic directions will be discussed.

Brenda Banwell
Children's Hospital of Philadelphia
Division of Neurology

Thomas Berger

«Since 2018 I'm Professor of Neurology and Chair of the Department of Neurology, Medical University of Vienna, Austria. My scientific interests concern inflammatory demyelinating CNS disorders, such as MS, NMOSD and MOGAD with a specific aim of clinical and laboratory biomarkers to aid / enable individualized and personalized approaches in patient care and management.
In addition, I'm honoured of serving as current president of the Austrian Society of Neurology and having been appointed member of the Austrian Supreme Public Health Council. Finally, I chair with enthusiasm the Scientific Committee of the European Academy of Neurology.»

MS in the Elderly – Immunosenescence and Implications for Management

Why should we draw our attention on elderly people with Multiple Sclerosis (pwMS)?
For several important reasons:

- Life expectancy in MS is nearly equal to matched population – thus, the group of elderly pwMS is continuously increasing
- The mean age of pwMS in clinical routine cohorts is approx. 55 years and approx. 25% of these pwMS are older than 65 years
- Increasing biological age does also affect our immune system, thus termed immunosenescence
- Immunosenescence may cause immune system dysregulation, with the consequence of e.g. increased susceptibility of infections, reduced vaccine immune responses, etc.
- Increasing biological age does also increase the likelihood of other diseases, for pwMS this accounts for a risk of concomitant disorders
- Ageing of pwMS self explains longer MS disease duration and with this regard it is well known (from former natural history studies) that inflammatory MS disease activity (relapses, MRI activity) decreases, whereas disease progression may increase (also as an MS-independent matter of ageing…)

All these facts impact care management of ageing and elderly pwMS:

a) Apart from specific MS care / management it is highly important to also consider management of other concomitant diseases / their risk factors to avoid any age-dependent and, thus, MS-independent factors that may add substantially to MS-independent health status worsening
b) Careful use of disease modifying therapies (DMT) with regard to consequences of immunosenescence, lack of approval for nearly all DMT in pwMS older than 55 years, unknown modes of action of available DMT in elderly pwMS, potential higher risk of adverse events / risks of DMT in aged pwMS, thus different benefit-risk evaluation as compared to youger pwMS, and, finally, considerations for decisions regarding stopping DMT.

Thomas Berger
Medical University of Vienna
Department of Neurology

rehaklinik
ZIHLSCHLACHT

We bring you back to the things you love

Specialist clinic for MS rehabilitation and neurological rehabilitation. Switzerland's leading provider of robot-assisted movement therapy.

Rehaklinik Zihlschlacht
Hauptstrasse 2 · CH-8588 Zihlschlacht
Tel. +41 71 424 33 33 · info@rehaklinik-zihlschlacht.ch
www.rehaklinik-zihlschlacht.ch

A healthcare facility of VAMED
health.care.vitality.

Workshops

Workshop A
13.30 – 14.15

Claudia Witt, Zürich & Ursula Wolf, Bern
Complementary Medicine:
Matching Patient Preferences and Evidence

Based on the concept of the three pillars of evidence-based medicine (patient preferences / beliefs; practitioners experience; best available evidence from clinical research), examples for complementary therapies within the approach of integrative medicine will be introduced and opportunities and challenges for implementation in the treatment of MS patients will be discussed.

Workshop B

13.30 – 14.15

Anne-Katrin Pröbstel, Basel &
Mireia Sospedra, Zurich
Nutrition and Microbiome:
Does MS start in the Gut?

Data from experimental and clinical studies point towards a key role of the gut microbiome in shaping the active immune response in MS. In this interactive workshop, we will discuss recent discoveries in regard to gut microbiota-immune interactions in MS and critically review current evidence for modulating the microbiome through dietary interventions.

14.15 – 14.30

Coffee Break

Workshop C/D/E

14.30 – 15.15

Covid-19 – What we know Today

Covid-19 has a tremendous impact on our whole society. Patients with autoimmune diseases like MS are specifically affected. In this workshop we will discuss the risks associated with a SARS-CoV2 infection in MS patients and the rationale for vaccination in DMT treated and untreated MS patients.

This workshop will be held parallel in German, French and Italian.

Tobias Derfuss, Basel & Anke Salmen, Bern
Workshop C: German

Renaud Du Pasquier & Oriol Manuel, Lausanne
Workshop D: French

Lara Diem & Giuseppe Locatelli, Bern
Workshop E: Italian

Claudia M. Witt

«Trained as a medical doctor and epidemiologist, I work as full professor at the Medical Faculty of the University of Zurich (UZH) and as Director of the Institute for Complementary and Integrative Medicine at the University Hospital Zurich. Our Institute is a Cochrane Complementary Medicine Satellite. At the UZH I serve as the head of the doctorate program for Care and Rehabilitation Science and as Co-Director of the Digital Society Initiative and Citizen Science Center. My research focuses on the evaluation of mind and body interventions for integrative and digital health and acupuncture. In my clinical work I apply the framework of Mind Body Medicine to patients with chronic diseases.»

Workshop A

Complementary Medicine: Matching Patient Preferences and Evidence. Acupuncture and Mind Body Medicine

Patients with chronic diseases such as MS are often interested in complementary medicine interventions. They have different reasons for the usage, and taking a more active role in their own treatment journey is an important one for them. There is a wide range of complementary medicine interventions, and this workshop presentation will focus on acupuncture and Mind Body Medicine.

The interventions will be introduced, examples for research will be presented and opportunities and challenges of the implementation in clinical care will be discussed.

Acupuncture is part of Chinese Medicine and widely used in Switzerland. When provided by medical doctors who are specialized in acupuncture (trainings provided by ASA) it is covered by the basic health insurance. When provided by non-medical practitioners, acupuncture can be covered by supplementary insurance contracts.

Mind body interventions include mindfulness, physical activity (e.g. yoga and qigong), relaxation exercises, breathing techniques, diet and self care interventions (e.g. acupressure). The conceptional framework of Mind Body Medicine, introduced by Herbert Benson at Harvard Medical School in the 1960s, and its further development (provided at the University Hospital Zurich in Switzerland since 2014), aims to improve symptoms and strengthen self care and self-efficacy in chronically ill patients. Taking the patients' preferences and beliefs into account when identifying the best possible treatment option for an individual patient is part of Evidence Based Medicine and plays a very important role in Mind Body Medicine. Because many mind body inter-

ventions are based on life style changes, it is part of the process to evaluate patients' preferences and experiences but also motivational aspects as described by the health action process approach (HAPA). Furthermore, individually adapted behavioral change techniques (BCTs) are used to support the implementation of the interventions. Mind Body Medicine can be applied in individual and group consultations by trained health professionals. The university training (CAS in Health Psychological Lifestyle Change and Mind Body Medicine, UZH) and the Swiss Association for Mind Body Medicine support the quality of the providers.

Claudia M. Witt
University Hospital Zurich
Institute for Complementary and Integrative Medicine

Notes

Ursula Wolf

I am a professor at the Medical Faculty of Bern and the Director of the Institute of Complementary and Integrative Medicine IKIM, University of Bern, where I teach, research and see patients (out-patients and in-patients). I am Board-certified in general internal medicine and anthroposophic medicine and have a long standing and broad clinical experience including intensive care, obstetrics, surgery and internal and A&E medicine. The focus of my research is on investigating effectiveness and safety of medication and non-medication complementary and integrative therapies. Besides my clinical training, I've spent 2.5 years in research in the USA, including neuroscience research. I am the current president of the International Society for Traditional, Complementary and Integrative Medicine Research ISCMR and the current president of the International Society on Oxygen Transport to Tissue (ISOTT).

Workshop A

Complementary Medicine: Complementary and Integrative Medicine in patients with MS

The use of complementary and integrative medicine (CIM) in Switzerland is high, i.e. up to 90% depending on the clinical indication, and 67% of the population voted for CIM in a referendum. Likewise, patients with MS often seek advice from CIM. Patients turn to CIM not because they are opposing to conventional therapies, but because they often have questions such as «What can I contribute to getting better?» or «What can I do to strengthen my resources and my self-healing forces?». In this workshop, we will, based on basic considerations and concrete case vignettes, discuss CIM treatment options, with an emphasis on anthroposophic medicine and Western phytotherapy. These, along with traditional Chinese Medicine and homeopathy, are covered by the basic health insurance if provided by physicians with a medical specialist title and a certificate of proficiency in the respective CIM field (German: Facharzttitel und Fähigkeitsausweis SIWF). Non-pharmacological treatments are reimbursed by supplemental health insurances. Western phytotherapy makes use of plant derived medication containing multicomponent mixtures. Practicing anthroposophic medicine requires a completed medical university training and degree. In anthroposophic medicine patients are considered holistically including their physical body, vital forces, soul and mind/spirit as well as their social functions. Anthroposophic medicine

enables a broad spectrum of treatments including medication and non-medication therapies, such as arts therapies, massage and eurythmy therapy (a mindful movement therapy). These therapies are well suited to address the above described needs of MS patients. At the IKIM, we observe in the medical consultations with the patients, all aspects of evidence-based medicine, i.e. the best available external evidence, the patient's preferences and the level of the physician's expertise. With an inter-professional approach, together with our colleagues from neurology and other medical disciplines, we establish individual treatment plans. In this workshop treatment options, clinical experiences, safety of the treatments, challenges, and patients' experiences and opinions will be shared and discussed with the participants.

Ursula Wolf
University of Bern
Institute of Complementary and Integrative Medicine

Notes

Anne-Katrin Pröbstel

«I am a senior physician and research group leader in the Multiple Sclerosis Center at the University Hospital Basel and was recently appointed as SNF Eccellenza Professor. My research group works on elucidating how gut microbiota are shaping specific immune cells (B cells) in MS with the aim to harness gut microbiota-immune interactions for the development of novel therapeutic strategies that target the gut microbiota composition.»

Mireia Sospedra

«I am an immunologist working as independent investigator in the Neuroimmunology and Multiple Sclerosis Research Section at the University of Zurich. My main focus of interest is T cell specificity in MS. Recently, my group has identified a new autoantigen in MS called GDP-L-fucose synthase. Reactivity against this autoantigen has revealed a putative role of gut microbiota as trigger of pathogenic T cells in MS and a putative link between diet and disease pathogenesis.»

Workshop B

Nutrition and Microbiome: Does MS start in the gut?

We have been observing a dramatic rise of multiple sclerosis cases in Switzerland and worldwide over the last decades. Given that the genetic architecture of the population does not rapidly change, mounting evidence points towards a key role of the environment in disease risk and progression. In that regard, data from experimental and clinical studies points towards a key role of the gut microbiome in shaping the active immune response in MS.

In this interactive workshop, we will discuss recent discoveries in regard to gut microbiota-immune interactions in MS and critically review current evidence for modulating the microbiome through dietary interventions.

Anne-Katrin Pröbstel
– University Hospital Basel
Neurologic Clinic and Policlinic
– University Hospital and University of Basel
Research Center for Clinical
Neuroimmunology and Neuroscience (RC2NB)

Mireia Sospedra
University of Zurich
Neuroimmunology and Multiple Sclerosis
Research

Anke Salmen

«As deputy head of the Ambulatory Neurocenter and head of Infusion Unit at the Inselspital, University Hospital Bern, where I work since 2016, I am engaged in the diagnosis and treatment of patients with Multiple Sclerosis (MS) and other demyelinating CNS disorders. My research group focuses on antibody-driven CNS disorders and visual outcome parameters in model systems as well as clinical-translational research in the field of MS, Neuromyelitis optica spectrum disorders (NMOSD) and MOG-IgG-associated disorders (MOGAD). With the Covid-19 pandemic, we have not only seen our neuroimmunological patients confronted with new challenges, but have also started to follow patients after Covid-19 infection suffering from sequelae such as fatigue and other symptoms.»

Tobias Derfuss

«I am a clinical neurologist with a specialisation in neuroimmunology. I received my clinical training at the Department of Neurology, Klinikum Grosshadern in Munich. Since 2010 I am professor and senior physician at the Department of Neurology and research group leader at the Department of Biomedicine of the University Clinic in Basel. My main research focus is the discovery of biomarkers and analysing the mode of action of disease modifying treatments in neuroinflammatory diseases. Especially the role of B cells in the pathogenesis of MS and the interaction of B cells with their target cells is explored in cell culture as well as in in vivo models. I am also involved in the design and conduct of clinical trials for newly emerging therapies in MS.»

Workshop C (in German)

Covid-19 – Was wir heute wissen

Die Covid-19-Pandemie beeinflusst unser persönliches und berufliches Leben nun seit fast 2 Jahren. Im Rahmen unseres Workshops möchten wir gemeinsam mit den Teilnehmenden eine lebhafte Diskussion über aktuelle Fragen führen.

Diese Fragen beziehen sich auf unsere MS- und andere neuroimmunologische Patienten im Hinblick auf die Immuntherapie und den Verlauf von Covid-19 bei diesen Patienten, sowie auf Impfstrategien. Wir möchten auch Auswirkungen der Pandemie

auf den Alltag unserer Patienten erörtern, etwa die Verschlechterung von Symptomen durch fehlende Physiotherapie oder psychologische Folgen.

Darüber hinaus berichten nicht nur unsere neuroimmunologischen Patienten, sondern auch Patienten, die «nur» von Covid-19 betroffen sind, häufig über anhaltende Symptome mit unterschiedlichen neurologischen Erscheinungsbildern. Es fehlt bisher an Betreuungs- und Behandlungsmöglichkeiten. Im Rahmen dieses Workshops wollen wir unsere Sichtweise und die aktuellen Daten und Erkenntnisse mit Ihnen teilen.

Anke Salmen
University Hospital Bern, Inselspital
Department of Neurology

Tobias Derfuss
University Hospital Basel
Neurologic Clinic and Policlinic

Notes

Renaud Du Pasquier
«I am the Head of Neurology at the CHUV in Lausanne. In addition to my clinical duties, I run a laboratory of Neuroimmunology with a focus on the immune mechanisms in Multiple Sclerosis and progressive multifocal leukoencephalopathy.»

Oriol Manuel
«I am an infectious diseases specialist and clinical researcher, working at the Infectious Diseases Service and the Transplantation Center of the Lausanne University Hospital in Lausanne. I am Associate Professor at the University of Lausanne. May main clinical and research interest is the prevention of infectious complications in immunocompromised patients.»

Workshop D (in French)

Covid-19 – Ce qu'on sait aujourd'hui

Il n'est nul besoin de rappeler l'impact énorme de la pandémie de Covid-19 sur nos vies depuis 2 ans. Cette maladie a des répercussions neurologiques non encore complètement élucidées. Il est donc important pour les neurologues d'être au courant des dernières données.

En outre, plus spécifiquement, la Covid-19 et la vaccination contre le SARS-CoV-2 peuvent avoir des répercussions significatives chez les patients SEP, en fonction de leur degré de handicap, de leur âge et du type d'immunomodulateur administré.

Renaud Du Pasquier
Lausanne University Hospital (CHUV)
Service of Neurology

Oriol Manuel
Lausanne University Hospital (CHUV)
Infectious Diseases Service

Lara Diem

«I am senior physician in neurology, active in the neuroimmunogical outpatient department at the Inselspital, University Hospital of Bern. My main clinical interest is Multiple Sclerosis and in particular vaccination and infections in patients with MS. Since December 2020, I have also been working on post-Covid-19 syndrome and am part of the expert board of the Altea information platform.»

Giuseppe Locatelli

«I am a biologist with 15 years of experience in academic research and more specifically in neuroimmunology and autoimmune inflammation. My research group at the University of Bern studies the pathological mechanisms behind multiple sclerosis using different animal models of disease. We are particularly interested in the dynamics of innate immune cells invading the central nervous system, and in the pathological degeneration of myelin during inflammation.»

Workshop E (in Italian)

Covid-19 e SM – Che cosa sappiamo

Il Covid-19 ha un altissimo impatto sulla nostra società. In particolar modo, pazienti affetti da patologie autoimmuni come la Sclerosi multipla sono sensibili alle conseguenze di questa malattia.

Tramite questo Workshop cercheremo di illustrare i rischi e le conseguenze legati all'infezione da SARS-CoV2 in pazienti affetti da sclerosi multipla, e discuteremo le ragioni per la relative vaccinazioni in pazienti sottostanti diverse terapie farmacologiche. Discuteremo inoltre delle ultime ricerche di laboratorio che descrivono la patologia Covid-19 e l'interazione di SARS-CoV2 con cellule immunitarie e cellule del sistema nervoso centrale.

Lara Diem, Bern
University Hospital Bern, Inselspital
Department of Neurology

Giuseppe Locatelli, Bern
University of Bern
Theodor Kocher Institute

MS Researcher Poster Presentations

The Swiss MS Society supports research projects in the field of Multiple Sclerosis with considerable financial contributions.

A selection of current projects is displayed in this abstract book

01 | Maud Bagnoud

Investigation of Vitamin D Signaling via the Glucocorticosteroid Receptor

Background — Several evidence suggest a beneficial effect of vitamin D (VD) on multiple sclerosis (MS) and its animal model, experimental autoimmune encephalomyelitis (EAE). Preliminary data from our group demonstrated that the beneficial effects of VD on EAE observed in wild type (WT) mice were lost in T cell specific glucocorticoid receptor (GR)-deficient mice suggesting a possible role of the GR in VD efficacy. In this study, we investigated if calcitriol, the active form of VD, signals via the GR in T cells to mediate its therapeutic effects in EAE.

Methods — Myelin oligodendrocyte glycoprotein (MOG35-55) EAE was induced in female C57BL/6JRj WT- and T cell specific GR-deficient mice. Four different concentrations of calcitriol (1-1000ng) were given orally after disease onset for three consecutive days. VD receptor (VDR) mRNA expression was measured ex vivo by real-time polymerase chain reaction in CD3+ T cells after calcitriol and MP treatment. The ability of calcitriol, calcidiol, methylprednisolone (MP) and dexamethasone (DEX) to bind to the GR was assessed through a LanthaScreen™ TR-FRET competitive binding assay. T cell apoptosis and T regulatory (Treg) differentiation were analyzed in vitro by flow cytometry with CD3+ T cells from both WT and T cell specific GR-deficient mice.

Results — Three days of calcitriol treatment (from 1ng/day to 100ng/day) significantly reduced EAE severity in WT mice whereas no beneficial effect was observed in T cell specific GR-deficient mice. In contrast, calcitriol treatment at a concentration of 1000ng/day worsened the disease in both genotypes. In vitro results showed

that calcitriol treatment significantly promoted apoptosis and Treg differentiation of CD3+ T cells from WT mice whereas these effects were abolished in CD3+ T cells from T cell specific GR-deficient mice, corroborating in vivo results. Biochemically, it was shown that MP and DEX, but not calcidiol and calcitriol, bind to the GR. However, a reduced VDR gene expression was observed in untreated T cell specific GR-deficient mice as compared to untreated WT mice ex vivo. This reduced VDR gene expression was abolished when mice were treated over three consecutive days with either calcitriol or MP.

Conclusions — Final results showed that calcitriol does not appear to signal directly through the GR but that the GR seems to be required for calcitriol signaling via the VDR, as the VDR is down-regulated if the GR is missing. To clarify this interaction further investigations are needed.

Research Team Members — Maud Bagnoud, Robert Hoepner

Maud Bagnoud
University Hospital Bern
Department of Neurology

02 | Sandra Bigi

The Swiss Paediatric Inflammatory Brain Disease Cohort Study:

Setting up a National Registry for Children and Adolescents with Paediatric Onset MS and Related Disorders

Background and rationale — Pediatric onset MS (POMS) is a severe disease affecting children and adolescents in a period of essential brain development. This possibly leads to early cognitive impairment, which may impact school performance and vocational achievements. Timely diagnosis and treatment initiation as well as individually tailored management are important for a favourable disease course/outcome. However, the diagnosis of POMS can be challenging, especially in young children, since their first demyelinating attack is often accompanied by unspecific symptoms also common to other inflammatory brain diseases (IBrainD). A systematic assessment of similarities and differences between clinical signs, symptoms, diagnostic workup, and management of POMS patients versus patients suffering from other IBrainD will enable faster and more reliable diagnosis. In Switzerland, there is neither epidemiological data nor information on health care management and disease outcome of POMS patients. Therefore, we are setting up a national registry, which will allow a deeper understanding of POMS epidemiology, clinical presentation, and management. Ultimately, the registry will improve the care of Swiss POMS patients.

Methods — Multicentre cohort study including prospective and retrospective data. Inclusion criteria: patients with POMS or another specified IBrainD with an onset before 18 years of age. Exclusion criteria: patients with 1) infectious diseases of the CNS; 2) genetic/metabolic causes of central demyelinating diseases; 3) neurological symptoms due to Guillain-Barré-Syndrome. Demographic and medical data are centrally collected.

Results — After the ethics committee approval by the end of 2020, ten out of the 11 participating centres have already been initiated. So far, we identified 194 potential participants with an IBrainD. Of those, 84 (43.3%) have a POMS diagnosis. Currently, 37 patients and/or families from seven centres have consented to participate in the registry. Retrospective patient identification was challenging due to a lack of systematic and unified coding approaches.

Conclusions — The national registry will answer pressing questions about the epidemiology and clinical phenotypes of POMS and related diseases in Switzerland. It also offers the opportunity to assess treatment and outcomes of paediatric IBrainD patients in a longitudinal fashion. Furthermore, the registry facilitates the national and international collaboration by providing a research platform.

Sandra Bigi
– *University Hospital Bern, Inselspital*
Department of Neurology and Department of Pediatrics
– *University of Bern*
Institute of Social and Preventive Medicine

03 | Jonas Bossart

Real-World Disease-Modifying Therapy Usage in Persons with Relapsing-Remitting Multiple Sclerosis:

Cross-Sectional Data from the Swiss Multiple Sclerosis Registry

Background — Several disease-modifying therapies (DMTs) have been approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). However, little is known about the current real-world treatment situation in Switzerland. Based on data from a diverse population of 668 persons with RRMS from the Swiss Multiple Sclerosis Registry (SMSR), the present study aims to fill this gap with a descriptive, cross-sectional approach.

Methods — Information on current health status and life situation in the last 6 months were extracted from the survey distributed throughout 2020 and 2021, while data on disease-modifying therapy (DMT) histories were included from preceding follow-up surveys. Initially, data were stratified into three DMT groups according to the current DMT status (NO (No DMT), CONTINUED (DMT started more than 6 months ago, which includes DMT continued at least until the date of survey response as well as DMT stopped or interrupted within the 6-month timeframe), and NEW (DMT started less than 6 months ago)). In a subsequent analysis, sample was stratified into groups corresponding to the five most frequently prescribed DMTs. Self-reported outcomes including therapy discontinuation or interruption, relapses and side-effects in the last 6 months were analysed per group. Life and health situation parameters were also analysed.

Results — The study covered 445 (66.6%) individuals belonging to the CONTINUED, 84 (12.6%) to the NEW, and 139 (20.8%) to the NO group. Within the NO group, 24 (17.3%) reported relapses. Furthermore, relapses (28 (33.3%)), side-effects (39 (46.4%)), and treatment discontinuations or interruptions (30 (35.7%)) were reported more frequently in the NEW when compared to the CONTINUED group (37 (8.3%), 125 (28.1%), 8 (1.8%), respectively). The three groups also differed with respect to age, time since diagnosis, number of symptoms, DMT history, and health-related quality of life. The five most frequently prescribed DMTs included fingolimod (33.4%), dimethyl fumarate (25.0%), ocrelizumab (23.6%), natalizumab (10.6%) and teriflunomide (7.5%). The frequency

of self-reported relapses ranged from 9.7% to 13.6%. Notable differences were found in the number of self-reported side-effects, ranging from 9.1% with natalizumab to 56.7% with dimethyl fumarate.

Conclusions — This cross-sectional analysis suggested that the majority of individuals with RRMS in Switzerland continuously receives DMT. However, sizable groups of persons not receiving DMT or groups struggling with side-effects or continued disease worsening while on DMT still persist. Injectable DMTs no longer play a major role in the treatment of RRMS in Switzerland, and a trend toward an early use of potent drugs is emerging.

Jonas Bossart
University of Zurich
Epidemiology, Biostatistics & Prevention Institute

04 | Donatella De Feo

Moncyte-Derived Oxidative Stress contributes to Neural Tissue Damage during Chronic Neuroinflammation

Background — Mononuclear phagocytes constitute a dominant fraction of CNS-infiltrating leukocytes found in lesions of multiple sclerosis (MS) patients. Genetic interference models have demonstrated that CCR2-expressing monocytes are the main drivers of CNS immunopathology in experimental autoimmune encephalomyelitis (EAE), the animal model of MS, while a subset of inflammatory microglia has been recently identified at the leading edge of chronic active demyelinating lesions associated to MS progression. Among the pathogenic equipment of phagocytes, reactive oxygen species (ROS) production have been associated to neurodegeneration.

Methods — We applied high dimensional spectral flow cytometry coupled with the ROS tracer, DCFDA, to characterize at single cell level the sources of oxidative stress in EAE CNS. To dissect the individual contribution to neuroinflammation and neurodegeneration of oxidative stress derived from each identified phagocyte subset, we systematically deleted, by conditional gene targeting, the NADPDH oxidase 2 (NOX2), the main enzyme involved in phagocytes' ROS biosynthesis, throughout the myeloid lineages.

Results — Firstly, we confirmed that monocyte-derived cells (MdCs) are the highest ROS producers among inflamed CNS mononuclear phagocytes, although also glial cells and neutrophils contribute to the oxidative stress burden associated to neuroinflammation. Functionally, EAE progressed normally when CNS resident phagocytes were genetically and functionally hampered in ROS production. Instead, deletion of Nox2 gene also in CX3CR1+ short-living HSC-derived phagocytes, upon disease onset, leads to a significant clinical amelioration of the chronic EAE course. ROS-silencing in monocytes and their progenies, via the CCR2-CreERT and Ms4a3-Cre monocyte-specific strains, during the chronic phase of EAE, phenocopied the clinical improvement obtained with the pan-phagocytes targeting approach.

Conclusions — These results indicate that ROS production by monocytes and MdCs is a relevant pathogenic mechanism for neural tissue damage underlining neuroinflammatory progression.

Donatella De Feo
University of Zürich
Institute of Experimental Immunology

05 | Samuel Jones

Identification of Brain-Autoreactive CD8+ T Cells using Autologous hiPSC-Derived CNS Cells

Background — Multiple sclerosis (MS) is commonly regarded as an autoimmune disease driven by autoreactive T cells but the interactions between the central nervous system (CNS) and immune cells are still poorly understood. Despite numerous research efforts in the field, it is still largely unknown how the immune system causes demyelination and no auto-antigen has yet been formally identified. This situation is partly due to the very limited access of brain tissue from MS patients hereby rendering the targets of T cells too elusive to conduct an unbiased antigen (Ag) screening.

Methods — Our objective is to develop a platform to identify autoreactive CD8+ T cells recognizing autologous brain cells, i.e. neurons, astrocytes and oligodendrocytes. To do so, we have developed an in vitro system to generate large amount of CNS cells based on human induced pluripotent stem cells (hiPSCs) derived from any donor. Using these cells, we have designed a co-culture assay to assess the activation of CD8+ T cells by Ags presented by autologous CNS cells. To detect activated CD8+ T cells, these cells were stained with dual specificity antibodies anti-CD45 and IFN-□. Upon activation, CD8+ T cells secrete IFN-□, which is captured by the antibodies then stained with a fluorophore-labeled anti-IFN-□ antibody. The frequency of activated CD8+ T cells is then assessed by flow cytometry.

Results — First, we have developed protocols to obtain enriched cultures of neurons, astrocytes and oligodendrocytes. Second, we demonstrated that these cells respond to IFN-γ by increasing their Ag-presenting capacity and upregulating MHC class I molecules at the cell surface. Third, in co-culture with au-

tologous CD8+ T cells, CNS cells pulsed with peptides are able to trigger activation of cognate Ag-specific CD8+ T cells. Finally, we demonstrate the capacity of CNS cells to elicit activation of Ag-specific CD8+ T cells through presentation of endogenously produced proteins in association with MHC class I molecules at membrane surface.

Conclusions — Overall, we now have at hand a tool allowing us to generate a complex autologous co-culture system between immune and CNS cells from any MS patient. This technique now validated, we will use this platform to assess the presence and frequency of CD8+ T cells targeting CNS Ags in a cohort of MS patients versus healthy donors. Ultimately, we will be in a position to identify Ag that would be specifically recognized in MS thus shading light on an important question of MS pathogenesis.

Research Team Members — Samuel Jones, Sylvain Perriot, Diane Bégarie, Mathieu Canales, Larise Oberholster, Marie Théaudin2, Caroline Pot, Amandine Mathias, Renaud Du Pasquier

Samuel Jones
– *University of Lausanne*
Laboratory of Neuroimmunology
– *Lausanne University Hospital (CHUV)*
Service of Neurology

06 | Vasileia Kalaitzaki

Peptide-Coupled RBCs as Treatment for Autoimmune Diseases – Dissecting the Mechanisms of Immune Tolerance Induction

Background — Induction of antigen-specific immune tolerance is one of the most specific ways of reverting the abnormal immune reactions commonly seen in autoimmunity. Our group has developed an antigen-specific therapy for the treatment of Multiple Sclerosis (MS), which involves the coupling of autologous red blood cells (RBCs) with a cocktail of seven MS immunodominant peptides from three myelin proteins. A recent phase Ib clinical trial in MS patients demonstrated its safety and tolerability and provided evidence for induction of immune tolerance in patients. Prior data suggest an indirect mechanism of immune tolerance induction, where peptide coupled RBCs (pcRBCs) are phagocytosed and processed by tissue-resident macrophages of the liver and the spleen, which present the antigens in a tolerogenic way. Here, we aim to elucidate the mechanism of action of this antigen-specific therapy.

Methods — We have established a reliable protocol for the in-situ digestion of mouse liver and the subsequent isolation of non-parenchymal cells, primarily liver macrophages. Additionally, we have developed a robust flow cytometry protocol for the identification and phenotypical characterization of these populations.

Results — So far, we have identified a CD11b+F4/80+ cell population, other than the CD11b+F4/80hi population of tissue-resident macrophages (Kupffer cells), which appears in the liver of mice, 2, 5 and 17 hours post intravenous injection with pcRBCs, and coincides with an increase in CD11b+F4/80- monocytes and a decrease in tissue-resident Kupffer cells. All three populations seem to be able to phagocytose the

injected pcRBCs, with Kupffer cells being the predominant phagocytosing population. Lastly, upon erythrophagocytosis, the Kupffer cell population seems to acquire a tolerogenic phenotype, displayed by the reduction in CD80 and MHCII molecules, while the newly appearing CD11b+F4/80+ cells seem to resemble the Kupffer cell population, as shown by the expression of MHCII, PD-L1 and the engulfment receptor TIM4.

Conclusions — Collectively, we have successfully established a model system for the study of peptide-coupled cell-mediated immune tolerance in vivo. We have phenotypically characterized the liver myeloid cell compartment and have identified the involvement of Kupffer cells in peptide-coupled cell phagocytosis. Moving forward, our focus will lie on the in-depth phenotypical and transcriptional characterization of the pcRBC phagocytosing populations, with the end goal of understanding the establishment of peptide-coupled cell induced immune tolerance.

Vasileia Kalaitzaki
– University Hospital Zurich
Neuroimmunology and Multiple Sclerosis Research
– University of Zurich
Institute of Laboratory Animal Science

07 | Antonios Katsoulas

Targeting CARD9-Mediated Signaling for Treatment of Multiple Sclerosis

Background — Multiple sclerosis is an inflammatory autoimmune disease of the CNS caused by undetermined environmental risk factors and specific polymorphisms in genes of the immune system. The most challenging part of the disease is the progression stage, where most irreversible damage occurs. Currently, most treatments are of limited use in the progressive forms of MS, emerging the need for more specifically designed treatments targeting novel cellular and molecular pathways. Notably, mounting evidence suggests that innate immunity plays a key role in MS development and progression.

Methods — Previous work of our lab identified the involvement of CARD9-mediated signaling in CNS autoimmunity using the experimental autoimmune encephalomyelitis (EAE) model (active and passive) in CARD9-deficient (CARD9-/-) mice, as well as multiparametric flow cytometry for cellular population analysis.

Results — We found that CARD9-/- mice have lower percentages of myeloid cells in the spleen in naïve state and are resistant to EAE. We determined that the requirement of C-type lectin receptors (CLR) in driving EAE is directly linked to the myeloid compartment of the CNS, probably the microglia. Surprisingly, despite CARD9-/- mice exhibiting EAE resistance, their T cells are capable of adoptively transferring disease to WT mice.

Conclusions — In conclusion, we have identified that CARD9 deficiency results in significantly ameliorated CNS autoimmunity in the EAE model of MS and we speculate that this is linked to the CNS-myeloid compartment. Moving forward, we will focus on exploring the cellular and molecular mechanisms through which CARD9-dependent signaling controls EAE development and proving that the CARD9 pathway is indeed a therapeutically relevant target. Currently, we are conducting in vitro validation of CARD9-targeting compounds in different types of mouse myeloid cells, prior to their in vivo administration as treatment of EAE. Our end goal is to evaluate whether the findings of CARD9 relevance in EAE mice can be translated to humans with progressive MS and thus, lay the groundwork for further development of a CARD9-based therapeutic approach not only in MS but also in other autoimmune diseases.

Antonios Katsoulas
University of Zurich
Institute of Laboratory Animal Science

SFCNS Swiss Federation of Clinical Neuro-Societies

YouCliN

5th SFCNS Congress

Swiss Federation of
Clinical Neuro-Societies

Transforming Education and Healthcare in the Digital Age

September 28-30, 2022

Congress Center Basel

sfcns2022.congress-imk.ch

Organized by IMK Institute for medicine and communication Ltd

08 | Myrta Kohler, Verena Witzig-Brändli

Development of a Nursing Counselling Intervention to Promote Self-Management of MS Patients in Rehabilitation

Background — Persons with Multiple Sclerosis (PwMS) have recurrent stays in rehabilitation clinics due to their progressive disease. During their time in rehabilitation, nurses are key players in supporting PwMS through self-management interventions. However, little is known about the effectiveness, adaptation to daily life and sustainability of these interventions. Therefore, the aim was to develop a nursing counselling intervention to support PwMS in their self-management goals, regardless of whether they are staying at home or are inpatients in the rehabilitation clinics.

Methods — We designed this intervention based on the Medical Research Council (MRC). With a systematic review we identified the best available data. We deepened our understanding of the context through qualitative interviews with PwMS (n = 15) and with focus group interviews with health care professionals (HCPs) (n = 8). To establish the goals of the intervention, we drew on existing theories. A program theory described how our intervention is expected to lead to its effect and what is needed. The core element of the intervention is a counselling guideline that was pilot tested (n = 5) and refined by PwMS (n = 6).

Results — The systematic review found little evidence of the effectiveness of a nurse-led counselling intervention for PwMS. The qualitative interviews indicated that in a continuous patient nurse relationship, nurses serve as advocates, representing PwMS' wishes and needs to HCP's. According to HCPs, nurses are knowledge-holders (e.g. they know patient information) but they are also knowledge carriers (e.g. they bring patient information to and from the HCP). After studying the context, the existing theories (self-management, caring, nurse consultation) and conducting a program, we developed a counselling guideline with two

parts (i) to assess PwMS as experts on their disease (ii) supporting them to set individual goals and actions to improve their self-management. The five PwMS in the pilot study rated their mean satisfaction of 95 % and all would reuse the intervention. PwMS feedback suggest the importance of nurse support in adaption self-management actions after rehabilitation to their daily lives.

Conclusions — Development using the MRC framework has created a theory-based intervention that is well embedded in the context. Further research on effectiveness is planned.

Myrta Kohler
– *Eastern Switzerland University of Applied Sciences*
Institute of Applied Nursing Science
– *Clinics of Valens*
Rehabilitation Centre Valens

Verena Witzig Brändli
Eastern Switzerland University of Applied Sciences
Institute of Applied Nursing Science

09 | Amandine Mathias

Multiparametric Phenotyping of Immune Cell Dynamics under Ocrelizumab:

A One-Year Longitudinal Study in MS Patients

Background — Depleting CD20+ B cells is the primary mechanism by which ocrelizumab (OCRE) is efficient in MS patients. However, current knowledge on how OCRE affects other immune cell subsets directly or indirectly is missing.

Methods — To characterize longitudinally the dynamics of immune cell of MS patients under OCRE, we collected blood samples from 38 MS patients before OCRE onset and after 6 and 12 months (T6, T12). A 38-parameter panel was designed for mass cytometry analyses including B, T, NK and innate immune cell markers as well as CNS migratory markers. Viral-specific T cell responses were further assessed using the interferon-γ-enzymelinked immunospot assay upon CMV, EBV and FLU-stimulations.

Results — We first confirmed the depletion of all B cell subsets already at T6. Regarding the innate compartments, we found 1. an increase in classical CD14+CD16- and non-classical CD14dim CD16+ monocytes at T6 ($p=0.022$, $p=0.005$) but not at T12 ($p=0.158$; $p=0.097$); 2. a diminished CD56bright NK cell subset at T6 ($p=0.0016$) and T12 ($p=0.0016$). Although the total numbers of CD4 and CD8 T cells remained stable, we observed a loss in: 1. memory CD4+T cells subsets including CXCR3+ Th1 at T12 ($p=0.0002$) and CXCR5+PD1+ cTfh at T6 ($p=0.042$) and T12 ($p=0.0017$); and 2. central and effector memory CD8+ T cell compartment, especially CD45RO+CCR7+/-CD20+/- subsets, already at T6 ($p=0.031$), an effect which was exacerbated at T12 ($p<0.0001$). The loss of memory CD8+T cells was further correlated with a lower expression of CXCR3 (T6: $p= 0.008$; T12: $p<0.0001$) and a reduced anti-viral immune response observed at T6 ($p=0.011$) and T12 ($p<0.0001$). Of note, T lymphopenia induced by previous immunosuppressive treatment was prolonged over the period of the study, a reduced T cell number associated with a higher prevalence of repeated infections and/or a low or absent anti-viral CD8 T cell response tested.

Conclusions — Our study provides new mechanisms by which OCRE impacts immune responses besides B cell depletion. Indeed, OCRE induces a transient increase in innate immune cells and reduces the number of memory CD4 and CD8+T cell subsets, which are suspected to be pathogenic in MS patients.

Research Team Members — Vasiliki Pantazou, Sylvain Perriot, Mathieu Canales, Samuel Jones, Larise Oberholster, Raphaël Bernard-Valnet, Marie Théaudin, Caroline Pot, Renaud Du Pasquier

Amandine Mathias, Lausanne
University of Lausanne
Laboratory of Neuroimmunology

10 | Johanna Oechtering

Intrathecal IgM Synthesis is Associated with Spinal Cord Syndromes in Early Multiple Sclerosis

Background — Likewise intrathecal IgM synthesis and spinal cord lesions are strongly and independently associated with faster conversion from clinically isolated syndrome (CIS) to Multiple Sclerosis (MS) and a more severe disease course. We aimed to investigate if presence of IgMIntrathecal Fraction (IF) (IgMIF+) is associated with a spinal cord manifestation in a first demyelinating event.

Methods — We included 122 treatment naïve patients with a first demyelinating event suggestive of MS prospectively recruited between 2012 and 2019 in the SMSC and cerebrospinal fluid (CSF) biobanking study at the University Hospital Basel. The type of clinical syndrome (optic nerve, supratentorial, brainstem/cerebellum, spinal, multifocal) was reassessed in the context of a detailed medical history, physical examination including EDSS, visually, sensory and motor evoked potentials as indicated, cerebral and spinal MRI independently by two neurological consultants blinded for CSF results. The amount of an intrathecal IgG or IgM synthesis was expressed as the intrathecal fraction of the total measured isotype concentration in CSF (IgGIF, IgMIF) in %, according Reiber formula. Patients were categorized by presence (+) or absence (-) of IgGIF and IgMIF (> / = 0 %). Associations of a spinal versus (vs) non-spinal clinical syndrome (n=111; 5 patients were excluded due to non-classifiable type and 6 due to multifocal clinical syndrome localization) (independent variables, respectively) were separately investigated by logistic regression adjusted for age and sex with IgGIF+ (vs. IgGIF-) or IgMIF+ (vs. IgMIF-) as dependent variable. To avoid confounding by presence of IgMIF in IgGIF+ patients, associations with IgGIF+ were additionally analysed by excluding IgMIF+ patients (n=29). The different frequencies of spinal (vs non-spinal) clinical syndromes in IgMIF+ vs IgMIF- patients were compared by chi-square-test.

Results — In 103 (84.4 %) the identical clinical syndrome was independently assigned, in 14 (11.5 %) consensus was reached and in 5 (4.1 %) the clinical syndrome could not be unequivocally assigned. Unifocal clinical syndromes were present in 111 (91.0%) patients, while 6 (4.9%) had a multifocal presentation. Patients with a spinal (69.0% in the IgMIF+ vs 22% in IgMIF- patients, p<0.01) (vs non-spinal) clinical syndrome had a 8.36-fold higher odds of an intrathecal IgM synthesis (95%CI 3.03, 23.03; p<0.01; n=111). Numerically this was also observed for IgGIF+ (OR 2.33; 95%CI 0.97, 5.59; p=0.058; n=111), but was no longer visible after exclusion of IgMIF+ patients (OR 0.85; 95%CI 0.28, 2.59; p=0.778; n=82).

Conclusions — Presence of IgMIF is strongly associated with a spinal cord manifestation in early MS. These two characteristics might be mutual features of a distinct subgroup of MS patients which is associated with an increased disease activity and severity.

Johanna Oechtering
– *University Hospital Basel*
Neurologic Clinic and Policlinic
– *University Hospital and University of Basel*
Research Center for Clinical Neuroimmunology and Neuroscience (RC2NB)

11 | Amalric Ortlieb & Mohamed Bouri

First feasibility study of assisting walking with the lower limb exoskeleton AUTONOMYO

Background — People suffering from multiple sclerosis can experience mobility disorders due to impaired motor control and muscle spasticity. Training and assisted movement stimulates the motor system and can improve the motor functions while preserving the muscle tonus. Lower limb exoskeleton allows to promote verticalized activities and potentially lower the user's fatigue when doing simple tasks as walking on ground.

Methods — A clinical study is conducted with 8 MS patients with an EDSS score between 4.5 and 6.5 and with 12 control participants. Three sessions are conducted where the exoskeleton will be worn in average over 30 minutes. Two persons will be assisting the participant wearing the exoskeleton or a TAURUS type rollator is used to guarantee safety. The two first sessions start with a manual muscle test (MMT) and a spasticity evaluation (MAS), a 2-minute walk test (MWT) without the exoskeleton, a training session with the exoskeleton and a 2MWT with the exoskeleton. The last session consists in the study in a gait lab of the gait with and without the exoskeleton with kinematics and muscle activity recording.

Results — All participants with MS were able to walk while wearing the exoskeleton. Small elements of discomfort and poor fitting have been reported for improvement. No adverse events have been reported. The exoskeleton seemed to importantly correct compensatory movements, however kinematics and muscle activity are still under post-processing and analysis. Participants reported various effects such as recovery of numbness of a few hours or feeling of a big increase in the walking capacity.

Conclusions — While the administration of the exoskeleton is not satisfactory as it requires the support from two persons, this feasibility evaluation provided enthusiastic results regarding safety and impact of using such an exoskeleton device. Further work needs to be conducted to propose an easy to use solution and to demonstrate impact on the long term with continuous use.

Amalric Ortlieb
– *Lausanne University Hospital (CHUV)*
MySpace laboratory
– *EPFL Lausanne*
REHAssist

Mohamed Bouri
– *Lausanne University Hospital (CHUV)*
MySpace laboratory
– *EPFL Lausanne*
REHAssist

12 | Nadine Patt

High-Intensity Interval Training is well tolerated, shows good Adherence and improves Cardiorespiratory Fitness in Persons with Multiple Sclerosis –

Interim Analysis of a Randomized Controlled Trial.

Background — Persons with Multiple Sclerosis (PwMS) show reduced aerobic capacity and report fatigue as the most disabling symptom impacting their health-related quality of life (HRQoL). The aim of this study is to evaluate the effect of a multimodal therapy approach, including endurance training and patient education, during a 3-week inpatient rehabilitation stay, on HRQoL in PwMS at 6 months follow-up. Inpatient energy management education (IEME) + high-intensity interval training (HIT) (experimental group) is compared to progressive muscle relaxation (PMR) + moderate continuous training (MCT) (standard care at the Clinics of Valens).

Methods — Secondary data from this two-armed, single-blinded randomized (1:1) controlled superiority trial were analysed. 100 PwMS-related fatigue (EDSS ≤ 6.5) were recruited at the Valens clinic and performed either HIT (3x/week) + IEME (2x/week) or MCT (3x/week) + PMR (2x/week) during the 3-week rehabilitation stay. HIT consists of 5x 1.5-min high-intensive exercise bouts at 95–100% of the peak heart rate (HRpeak) followed by active breaks of unloaded pedalling for 2min at 60% of HRpeak on a cycle ergometer. MCT consists of 24-min continuous cycling at 65% of HRpeak. Cardiorespiratory fitness (peak oxygen consumption) was assessed at entry (T0) and discharge from the clinic (3 weeks, T1), by performing an incremental cardiopulmonary exercise test until exhaustion on a cycle ergometer. A 2 x 2 mixed analysis of variance (ANOVA) was applied to detect potential within (time) and interaction (time x group) effects. Adherence and motivation (subjective rating from 0-10) were recorded after each training session.

Results — Between July 2020 and October 2021, 100 PwMS were recruited. ANOVA revealed significant time effects ($p<0.001$) for cardiorespiratory fitness. The HIT group completed 6.74 (1.75) and the MCT group 7.56 (1.81) training sessions. Adherence to the prescribed training intensity of 95-100% of HRpeak was given for 44 (88%) participants in the HIT group. 5 (10%) participants were not able to train at the prescribed intensity (mean training intensity: 92.2% HRpeak). 1 (2%) participant was not compliant to the training protocol. In the MCT group adherence was given for all participants. Motivation was high in both groups (HIT: 7.98 (2.14), MCT: 7.48 (1.88)). HIT was well tolerated with no adverse events.

Conclusions — This analysis shows that HIT is safe and effective for improving cardiorespiratory fitness. The intervention is well tolerated and motivation is high.

Nadine Patt
Clinics of Valens
Rehabilitation Centre Valens

13 | Ines Pereira & Zina-Mary Manjaly

Mechanisms of Fatigue in Multiple Sclerosis –

Investigations with fMRI (FAMRI)

Background — Fatigue is one of the most frequent symptoms in multiple sclerosis (MS) and has a major impact on quality of life. At present, there do not exist any clinical tests that could guide treatment. As a consequence, therapy currently proceeds in a trial-and-error fashion. Since fatigue most likely has a heterogeneous pathophysiological basis, individualised treatment would require that we can detect the specific disease mechanism in each patient. Several potential disease processes have been identified that might be expressed variably (and possibly in combination) across persons with MS (PwMS), incl. (i) reduced monoaminergic projections from brainstem nuclei, (ii) diminished strength of orexinergic projections from the lateral hypothalamus, and (iii) altered interoception.

Methods — In the FAMRI study we obtain functional readouts that reflect the above pathophysiological mechanisms and investigate how well these measures explain the variability of fatigue across PwMS. To this end, structural and functional MRI (fMRI) and physiological measures (incl. sleep) will be obtained from PwMS (N=75) with variable degrees of fatigue. In order to assess brainstem projections, hypothalamic projections, and connections within the cortical interoceptive network, respectively, we will conduct fMRI analyses of «resting state» functional connectivity and use novel methods for whole-brain effective (directed) connectivity analyses. Furthermore, we will use structural MRI techniques sensitive to tissue damage (quantitative T2), examine abnormalities of interoception and autonomic regulation with questionnaires and physiological measures, and investigate the contribution of low sleep quality to fatigue with actigraphy.

Results — Applying statistical analyses and machine learning to these measures, we will test whether (i) individual levels of fatigue can be explained by a combination of readouts reflecting the proposed pathophysiological mechanisms, (ii) which of these measures shows the strongest relation to individual fatigue levels on its own, (iii) whether local tissue damage in regions of interest correlates with fatigue, and (iv) which functional connections across the whole brain correlate with fatigue levels.

Conclusions — If a clear relationship between any (or several) of the readouts reflecting proposed pathophysiological mechanisms and fatigue levels were found, this could provide a basis for testing whether imaging-based treatment selection could support individualised therapy of fatigue in MS.

Research Team Members — Ines Pereira, Reka Enz, Delania Meng, Laura Köchli, Nicole Zahnd, Stefanie Marino, Stefan Frässle, Klaas Enno Stephan, Zina-Mary Manjaly

Ines Pereira
University of Zurich & ETH Zurich
Translational Neuromodeling Unit

Zina-Mary Manjaly
Schulthess Clinic, Zurich
Department of Neurology

14 | Maximilian Pistor

Analysis of sex differences in the efficacy of Sphingosine-1-Phosphate Receptor modulating immunotherapies

Background — Sex-specific differences in treatment efficacies have been a neglected aspect in MS research, like in most other fields of medicine. Whereas sex differences in MS have been described in various other aspects, the pivotal studies of disease-modifying therapies (DMT) have mostly evaluated sex as a covariate or in subgroup analyses, but thus not investigated them independently. Fingolimod (FTY) and the more recently approved other Sphingosine-1 Phosphate Receptor Modulators (S1PRM) Siponimod and Ozanimod are one of the most frequently prescribed DMT for relapsing-remitting and secondary-progressive Multiple Sclerosis (MS) in Switzerland. We hypothesize that age and sex differences in systemic Sphingosine-1 Phosphate (S1P) levels, which are known to be partly dependent on estrogen levels and natural ligand and competitor of the S1PRM like FTY on the S1P-receptors, might contribute to differences in S1PRM efficacy.

Methods — For the first part, a cohort of Fingolimod and Dimethyl Fumarate treated pwMS was retrospectively analysed for the primary outcome «time to first relapse» by survival analysis. In the second part, within a pilot experiment of our collaboration partner, serum levels of S1P of FTY treated pwMS were assessed by mass spectroscopy. Finally, active MOG EAE was induced in C57BL6-mice. They were treated with S1P (10 ng) or normal saline (NaCl 0.9%) via subcutaneous injections to model higher systemic S1P levels. Treatment with FTY 0.005 mg/kg (in condensed milk) or condensed milk as vehicle control for up to 20 days was additionally used. Animals were assessed daily using a 10-point EAE score and followed up to 28 days. Histological assessment for T-cell, macrophage infiltration and demyelination was performed.

Results — In our cohort (n=616), female pwMS treated with FTY had a higher relapse risk compared to male pwMS (adjusted Hazard Ratio (aHR) 2.4; 95%-CI 1.2 – 4.6, p=0.001) whereas for Dimethyl Fumarate, no sex differences where observable (p>0.05). In FTY treated pwMS stratified by age (≤45 vs. >45 years), this effect could only be shown in women <45 years (aHR 3.3 (1.5-7.1), p<0.01). Serum levels of S1P of 16 FTY-treated pwMS (4 male, 12 female) were higher in female than male pwMS (492.4 (382.7 – 602.1) ng/ml vs. 311.4 (223.2 – 399.5), p<0.05). Finally, in S1P-treated mice, FTY was less efficient compared to NaCl treated mice as control (Area under the curve: 50.1 (43.9 – 56.3) vs. 43.9 (34.4 – 53.4, p=0.06; one individual EAE experiment, n= 6-8/group).

Conclusions — Our retrospective study demonstrates sex differences in the relapse risks of pwMS treated with Fingolimod as «first in class» of the S1P-receptor modulators. We hypothesize, that these differences might be, at least in part, due to higher S1P levels in female compared to male pwMS, which we could demonstrate in a small pilot experiment. Finally, we could demonstrate that higher S1P levels in EAE mice might interfere in FTY's efficacy in EAE. These first results need to be interpreted with caution, as both S1P measurements need to be replicated in larger cohorts as well as the EAE needs to be replicated. Additionally, we can at this point make no assumptions concerning the newer S1PRMs approved recently.

Research Team Members — Maximilian Pistor, Marine Massy, Maud Bagnoud, Anke Salmen, Robert Hoepner

Maximilian Pistor
University Hospital Bern, Inselspital
Department of Neurology

15 | Jana Remlinger

Comparative Investigation of Antibody- and Non-Antibody-Mediated CNS Autoimmunity

Background — In autoimmune demyelinating disorders of the central nervous system (CNS), visual system and spinal cord are prominent targets during disease attacks leading to potentially irreversible impairment. Comparative data on Multiple Sclerosis (MS), Neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein (MOG-) IgG-associated disorder (MOGAD) are widely lacking or thus far inconclusive. Here, we compare antibody- and non-antibody-mediated murine experimental models of CNS demyelination to increase the understanding of different pathomechanisms associated with antibodies against AQP4 and MOG as compared to a non-antibody-associated model system.

Methods — Murine chronic active MOG35-55 experimental autoimmune encephalomyelitis (EAE) was induced and AQP4-, MOG- or isotype IgG (Iso-IgG) were administered around onset of disease symptoms. Visual outcome was assessed longitudinally (baseline, acute and chronic disease phase) via optomotor reflex and optical coherence tomography. Histological correlates of disease in the spinal cord and optic nerve were quantified using immunohistochemistry for immune cell infiltrations, Luxol Fast Blue/PAS and myelin basic protein staining for demyelination and immunofluorescence for AQP4 and the astrocyte marker GFAP.

Results — Disease severity was highest after application of MOG-IgG compared to AQP4-IgG or Iso-IgG. Both, MOG-IgG and AQP4-IgG administration increased disease incidence compared to Iso-IgG. Visual acuity, but not retinal layer thickness decreased over the course of disease in both antibody-augmented models. Distribution of demyelination, macrophage and T cell infiltration in spinal cords was significantly different in AQP4-IgG as com-

pared to MOG- and Iso-IgG groups, and loss of grey matter myelin integrity was observed in deep ventrolateral lesions in all groups. In spinal cord, but not optic nerve, macrophage infiltration was increased in the acute compared to chronic disease phase. In a preliminary evaluation, intensity of specific markers of astrocytes and AQP4 in the spinal cord was reduced in AQP4-IgG compared to MOG-IgG EAE at acute but not chronic disease stage.

Conclusions — Even though antibody administration increased disease incidence, classical histopathological hallmarks in the chronic disease phase do not differ between the three groups, rather depicting the final stage of damage and clearance by macrophages. During the acute disease stage, pathophysiological differences between models are present. Different localization of the lesions potentially reflects different predilection sites of AQP4- vs. MOG- vs. non-antibody driven models. Loss of visual function was not reflected on a morphological level, but further histopathological analyses are ongoing and will be complemented by translational investigations in a human system using human organotypic retina cultures.

Jana Remlinger
University Hospital Bern, Inselspital
Department of Neurology

16 | Mina Stanikic

Association of Comorbidities and Disability with Age and Disease Duration:

Cross-Sectional Study of the Swiss Multiple Sclerosis Registry

Background — In addition to increasing the risk of developing comorbidities in the general population as well as in persons with Multiple Sclerosis (PwMS), ageing affects the course of Multiple Sclerosis (MS) (1). Thus, we are studying the independent associations of ageing and MS duration on the disability and comorbidity burden in the Swiss MS Registry (SMSR) (2).

Methods — Data of adult SMSR participants was used to cross-sectionally explore the association between age, MS disease duration and 6 outcomes of interest: cancer, hypertension, cardiac problems, type 2 diabetes (T2D), depression, and achieving disability milestone of the Self-Report Disability Status Scale (SRDSS) ≥ 4. All outcomes and measurements were based on self-reported data from the SMSR baseline and follow up questionnaires. Distribution of outcomes was descriptively compared across 6 age categories and 4 MS duration categories. Multivariable logistic regression models adjusted for sex, baseline MS type, body mass index, smoking and disease modifying treatment were used. Age and MS duration were included jointly as linear variables. Models also considered interaction terms for age and MS disease duration, which only improved the model fit for cancer and SRDSS >= 4 outcomes.

Results — Of 1'680 PwMS with no missing data 72.9% of the sample were women. Median [interquartile range] age was 47 [35, 77], and the majority of PwMS had relapsing-remitting MS (68.5%). Depression was the most often reported comorbidity (13.3%), followed by hypertension (12.7%) and 30.3% of the participants reached SRDSS of 4 or higher. Achieving disability equal to or higher than 4 on SRDSS was positively and independently associated with both age and MS duration. Participants became 1.67 times more likely

to achieve SRDSS ≥ 4 (OR 1.67, 95% CI [1.43, 1.95]) with each category of MS duration compared to the preceding category, and 1.46 more likely with each age category (OR 1.46, 95% CI [1.27, 1.67]). Contrary to this, having a comorbidity was not significantly associated with MS duration, while age was the main driver for hypertension and T2D, with more than a twofold increase in odds per category (OR 2.17, 95% CI [1.82, 2.58] and OR 2.11, 95% CI [1.35, 3.28], respectively). Furthermore, frequency of having cancer increased by 55% per age category (OR 1.55, 95% CI [1.10, 2.19]).

Conclusions — Reaching disability milestone of SRDSS ≥ 4 was associated with both age and MS disease duration, while the presence of cancer, hypertension and T2D was associated with age, but not MS duration.

References — (1) Sanai SA, Saini V, Benedict RH, Zivadinov R, Teter BE, Ramanathan M, et al. Aging and multiple sclerosis. Mult Scler J. 2016;22(6):717–25.
(2) Steinemann N, Kuhle J, Calabrese P, Kesselring J, Disanto G, Merkler D, et al. The Swiss Multiple Sclerosis Registry (SMSR): study protocol of a participatory, nationwide registry to promote epidemiological and patient-centered MS research. BMC Neurol. 2018;18(1):1–10.

Mina Stanikic
– *University of Zurich*
Epidemiology, Biostatistics & Prevention Institute
– *University of Zurich*
Institute for Implementation Science in Health Care

17 | Solenne Vigne

Targeting the Gut Microbiota to Modulate Th17 Cell Encephalitogenic Properties during EAE

Background — Multiple sclerosis (MS) is a chronic inflammatory and autoimmune disease affecting the central nervous system (CNS) leading to neuronal damage and debilitating neurological deficits. The aetiology of MS is multifactorial, and gut microbiota was identified as an emerging environmental factor involved in MS pathogenesis. In our laboratory, we showed using an adoptive Th17 cell adoptive transfer EAE mouse model, that CNS myelin-specific Th17 cells are first located in the gut at a preclinical stage of the disease where they proliferate near the colonic lumen. Moreover, we showed that CNS myelin-specific Th17 cells induce an alteration of the gut microbiota composition before reaching the CNS. In addition, blocking Th17 migration to the gut dampens EAE. Those results suggest an intrinsic relationship between CNS-specific Th17 cells and intestinal microbiota composition. However, the precise mechanisms of the gut flora-Th17 cells interaction remain to be studied.

Methods — To characterize the impact of intestinal microbiome modulation on CNS-specific Th17 cells in the gut, we took advantage of an EAE mouse model and adoptively transferred TCRMOG 2D2 Th17 cells in recipient mice that previously received antibiotics or not. We first assessed EAE disease development. In addition, we performed an RNA sequencing analysis of FACS-sorted colonic TCRMOG 2D2 Th17 cells 4 days after Th17 cell transfer. We evaluated TCRMOG 2D2 Th17 cell phenotypic profile and infiltration in the gut and the CNS by flow cytometry analysis. Finally, to evaluate the functional immunomodulatory effects of intestinal dysbiosis induced by antibiotics treatment on the TCRMOG Th17 cells in the gut, we directly extracted TCRMOG 2D2 Th17 cells from colonic lamina propria (CLP) and restimulated them in vitro in the presence of myelin peptide (MOG35-55).

Results — We show that preventing Th17-induced dysbiosis by antibiotic treatment dampens EAE. Those results suggest an intrinsic relationship between CNS-specific Th17 cells and intestinal microbiota composition. We identified in our RNA sequencing experiment several signaling pathways of the colonic Th17 cells that are significantly impacted by antibiotics treatment, specifically INF-□ signaling and chemotactic properties contributing to Th17 cell pathogenicity. We further show by qPCR analysis of 16S bacterial analysis, that the species Akkermansia muciniphila, previously reported to be increased in MS patients and EAE, could be implicated in shaping Th17 cell phenotype in the gut.

Conclusions — These results contribute to better understanding of how immune cells are regulated in the intestine and to reevaluate the gut as a target organ during CNS autoimmunity and multiple sclerosis.

Research Team Members — Solenne Vigne, Jessica Rebeaud, Benjamin Peter, Florian Ruiz, Valentine Bressoud, Caroline Pot

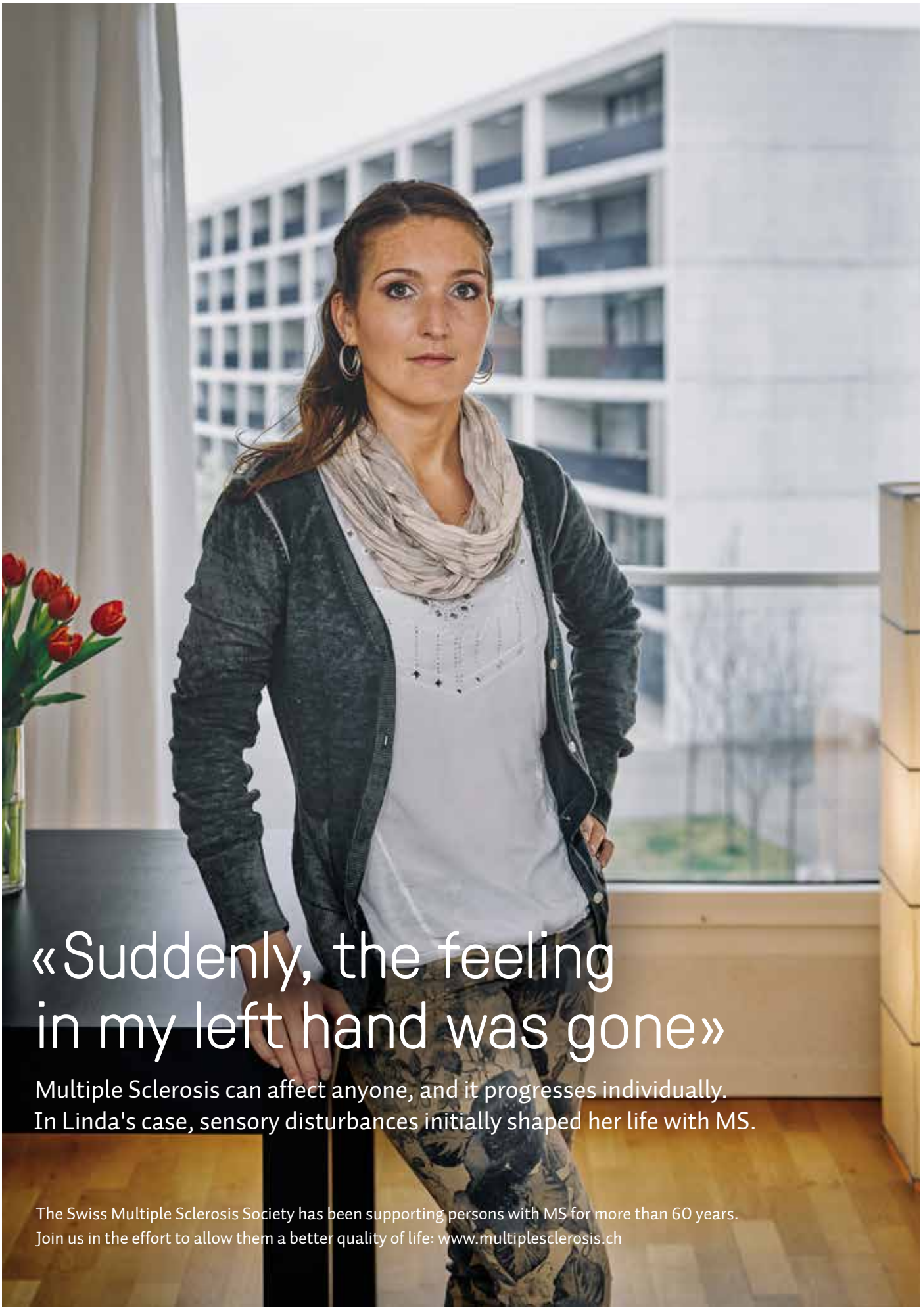
Solenne Vigne
– *Lausanne University Hospital (CHUV)*
Laboratory of Neuroimmunology
– *Lausanne University Hospital (CHUV)*
Service of Neurology

Caroline Pot
Lausanne University Hospital (CHUV)
Service of Neurology

We thank you for your participation in the symposium.

See you next year at the 25. MS State of the Art Symposium, Saturday, January 28, 2023.

Kind regards
Swiss Multiple Sclerosis Society



MS Swiss Multiple Sclerosis Society

Swiss Multiple Sclerosis Society

Josefstrasse 129 / 8031 Zürich
Information: www multiplesklerose.ch / 043 444 43 43
info@multiplesklerose.ch