

# Translational Neuro- immunology



**Matthias Mehling**

Department of Biomedicine  
und Neurology Clinic  
University Hospital Basel

## Group Members

Andrea Amstad\*  
(MD Student)  
Agathe Blanc\*  
(Intern)  
Divya Chaudhary\*  
(External Collaborator)  
Mali Cristina Coray  
(PhD Student)  
Corina Frick  
(External Collaborator)  
Friedrich Jakob Fuhrmann  
(MD Student)

\*left during report period

## Chemokines, atypical chemokine receptors and chemotaxis in multiple sclerosis

Migration of immune cells plays an important role in protective immunity but also in the pathogenesis of multiple sclerosis. Directed migration of immune cells is governed by chemokine gradients acting as extracellular guidance cues. During the last years we have developed various microfluidic devices to study migration properties of primary immune cells on a single cell level. These devices allow to generate precisely controllable stable diffusion-based and/or immobilized chemokine gradients of various shapes. This allows studying basic aspects of signal integration of migrating cells, including the question how cells sense the direction of chemokine gradients and what sustains migration along potentially irregular gradients in non-inflamed and inflamed tissues.

Consensus exists that chemokine gradients offer the main guidance cues for migrating immune cells. Only limited data is available regarding how such gradients are generated and maintained. Atypical chemokine receptors (ACKRs) are able to scavenge chemokines, hereby shaping the distribution of chemokines locally. The expression of chemokine-scavenging ACKRs in inflamed multiple sclerosis lesions suggests that ACKRs also play an important role in shaping chemokine distribution –and hence immune cell recruitment to sites of inflammation. We aim to understand, how expression of ACKRs on glial cells impacts on the distribution of chemokines in inflamed CNS tissue.

## Vaccinations, immunosenescence and multiple sclerosis

Vaccinations are important measures of global health, not only since the Coronavirus pandemic. Consensus exists that all persons with MS should be immunized according to the local vaccine standards.

Physicians and other healthcare providers caring for persons with MS are often faced with questions concerning vaccinations, particularly in patients receiving disease modifying therapies (DMTs). We aim at understanding how DMTs and also how treatment histories impact on vaccine responses. We further link these data to the degree of immunosenescence in individual patients, since immunotherapies can result in accelerated aging of the immune system.

## Connection to Clinical Practice

Our group is closely connected to the MS Centre and Outpatient Clinic of the Department of Neurology, University Hospital Basel that provides care for more than 1300 MS patients per year. Particularly, collaboration with the Swiss Multiple Sclerosis Cohort (SMSC, coordinated by Prof. Kuhle, Neurology Department of the University Hospital Basel) provides an internationally unique long-term follow-up of over 1200 Swiss MS patients with clinical and MRI data and serum samples for vaccine research. Prospective vaccination studies are organized in collaboration with the Vaccine Service of the Medical Outpatient Clinic, University Hospital Basel (coordinated by PD Dr. Ch. Berger).

## Selected Publications

- Amstad A, Coray M, Frick C, Barro C, Oechte-ring J, Amann M, Wischhusen J, Kappos L, Naegelin Y, Kuhle J, Mehling M. Growth differentiation factor 15 is increased in stable MS. *Neurol Neuroimmunol Neuroinflamm.* 2020 Feb 5;7(2):e675.
- Frick C, Dettinger P, Renkawitz J, Jauch A, Berger CT, Recher M, Schroeder T, Mehling M. Nano-scale microfluidics to study 3D chemotaxis at the single cell level. *PLoS One.* 2018 Jun 7;13(6):e0198330.
- Schwarz J, Bierbaum V, Merrin J, Frank T, Hauschild R, Bollenbach T, Tay S, Sixt M, Mehling M. A microfluidic device for measuring cell migration towards substrate-bound and soluble chemokine gradients. *Sci Rep.* 2016 Nov 7;6:36440.
- Dimeloe S, Mehling M, Frick C, Loeliger J, Bantug GR, Sauder U, Fischer M, Belle R, Develioglu L, Tay S, Langenkamp A, Hess C. The Immune-Metabolic Basis of Effector Memory CD4+ T Cell Function under Hypoxic Conditions. *J Immunol.* 2016 Jan 1;196(1):106–14.