Theodor Kocher Institute (TKI)

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Prof. Dr. Britta Engelhardt
Director and Research Group Leader

Prof. Ruth Lyck
Research Group Leader

Dr. Urban Deutsch
Research Group Leader

Dr. Gaby Enzmann
Principal Investigator

Dr. Giuseppe Locatelli
Research Group Leader

Dr. Steven Proulx
Research Group Leader

Profile

- The TKI hosts 5 research groups studying central nervous system immunity in health and disease with a focus on multiple sclerosis, stroke, Alzheimer's disease and brain metastasis of tumors by employing advanced in vitro and in vivo imaging aproaches
- TKI staff is involved in teaching bachelor and master students of the Medical, Science and Vetsuisse Faculties in lectures and practical classes in immunology, vascular and cell biology, transgenic mouse technologies as well as in advanced microscopy and image analysis. TKI staff also educates graduate students of the Graduate School for Cellular and Biomedical Sciences (GCB) and coordinates the national PhD program "Cell Migration" and the local PhD program "Cutting Edge Microscopy"
- External partners: Renaud Du Pasquier, CHUV, Lausanne; Harm-Anton Klok, EPFL, Lausanne; Michael Detmar, ETH Zurich; Thorsten Buch, University of Zurich; Vartan Kurtcuoglu, University of Zurich; Tobias Dick, Heidelberg, Germany; Martin Kerschensteiner, LMU Munich, Germany; Gianluca Matteoli, KU Leuven, Belgium; Marco Prinz, University Hospital Freiburg, Germany; Nicholas King, University of Sydney, Australia; Yann Decker, University of the Saarland, Germany; Eric Shusta, University of Madison-Wisconsin, Madison, USA; James McGrath, University of Rochester, NY, USA; Anne Astier and Roland Liblau, INSERM, Toulouse, France; Eric Thouvenaut, Montpellier, France

Grants

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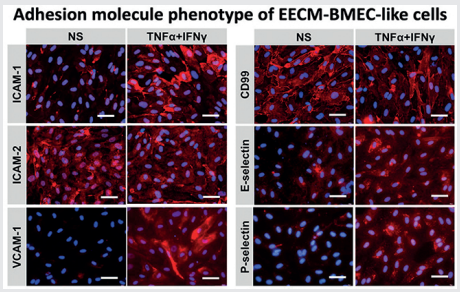
Highlights



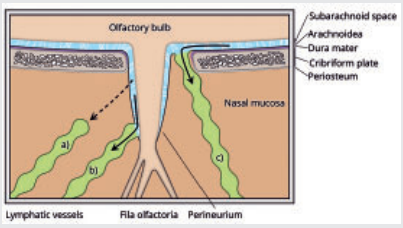
EECM-BMEC-like cells express cell adhesion molecules in a constitutive and cytokine inducible manner. Immunofluorescence stainings are shown. Nuclear stain blue, adhesion molecule red. Bar = 50 µm

Advancing human induced pluripotent stem cell-derived blood-brain barrier models for studying immune cell interactions

Current human induced pluripotent stem cell (hiPSC)-derived blood-brain barrier (BBB) models are not suited to study immune cell migration across the BBB in vitro. In a fruitful collaboration with the teams of Renaud Du Paquier (CHUV, Lausanne) and Eric Shusta (University of Madison Wisconsin, USA) we have established the novel extended endothelial cell culture method (EECM), which differentiates hiPSC-derived endothelial progenitor cells to brain microvascular endothelial cell (BMEC)-like cells with BBB properties. EECM-BMEC-like cells display functional expression of endothelial adhesion molecules mediating immune cell interaction under physiological flow. EECM-BMEC-like cells are the first hiPSC-derived BBB model with a mature immune phenotype.

Mapping the outflow of cerebrospinal fluid

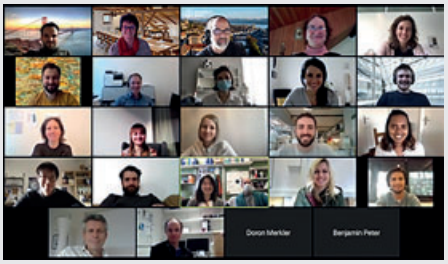
Our group has recently shown that cerebrospinal fluid (CSF) clearance from the central nervous system occurs through lymphatic vessels in mice. However, the exact anatomical routes of egress remain to be elucidated. We have established decalcification protocols in transgenic fluorescent reporter mice to demonstrate the anatomical pathways of CSF tracer clearance through the cribriform plate of the skull. Consistent with some historical reports, we have determined that pathways exist along the olfactory nerves as they penetrate through the cribriform plate towards the olfactory epithelium. Lymphatics within the nasal mucosa then drain the tracers to the deep cervical lymph node.



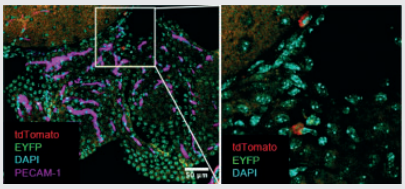
Scheme of proposed models of CSF outflow

Success stories during pandemic times

We have tried to efficiently use the extra homeworking time during 2020 to organize the Young Investigator Meeting, bringing together leading scientists from 11 different Swiss laboratories investigating the pathology of Multiple Sclerosis in humans and animal models.



A salute from the YIM participants



Choroid plexus from an iNOS-Arginase double transgenic reporter mouse model during neuroinflammation

Activated macrophages within the mouse choroid plexus

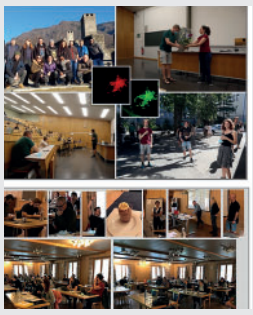
We investigated the trafficking and functional properties of macrophages within the Central Nervous System during autoimmune CNS inflammation, with a specific focus on the choroid plexus within brain ventricles. By using reporter mouse models expressing fluorescent proteins in distinct pro- and anti-inflammatory macrophages, we could thus describe increased trafficking of blood-derived macrophages and functional polarization of macrophages within the choroid plexus.

Ruth Lyck: Associate Professor

Ruth Lyck has been nominated Associate Professor of the University of Bern. Focusing her research originally on immune cell migration across the blood-brain barrier, Ruth has recently shifted her research focus on melanoma cell migration across tissue barriers. Ruth has worked part time during her entire career and is thus an excellent female role model for scientists in the future.

The PhD programs Cutting Edge Microscopy (CEM) and Cell Migration coordinated by Ruth Lyck and Britta Engelhardt, respectively, had the chance to organize in person meetings in 2020.

In February, PhD students of the CEM program visited the Institute for Research in Biomedicine in Bellinzona. In July, the core event of the MIC Summer school, the CEM Students' Day with scientific presentations, could take place under strict Covid-19 pandemic measures. The 8th Annual retreat of the Cell Migration Program took place from September 22-23, 2020 at the Seminarhotel Hirschen in Eggiwill in the Emmental. Despite the Covid-19 pandemic implemented measures, the students and their supervisors greatly enjoyed the direct interactions and discussions and had a wonderful time.



Activities of the PhD programs