

Theodor Kocher Institute (TKI)

Freiestrasse 1, 3012 Bern
www.tki.unibe.ch



Prof. 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
---	--	--	--	---	--

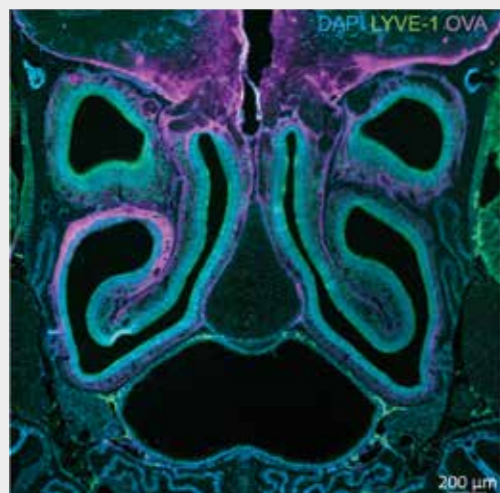
Profile

- 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 approaches.
- We are teaching bachelor and master students of the Medical, Science and Vetsuisse faculties in lectures and practical classes in immunology, vascular and cell biology. We are educating graduate students of the Graduate School for Cellular and Biomedical Sciences (GCB). We are coordinating national PhD programs "Cell Migration" and "Cutting Edge Microscopy".
- External partners: Renaud Du Pasquier, CHUV, Lausanne; Harm-Anton Klok, EPFL, Lausanne; Michael Detmar, ETH Zurich; Thorsten Buch, University Zurich; Tobias Dick, Heidelberg, Germany; Martin Kerschensteiner, LMU Munich, Germany; Gianluca Matteoli, KU Leuven, Belgium; Marco Prinz, University Hospital Freiburg, Germany; Nicholas King, University Sydney, Australia; Yann Decker, University of the Saarland; Eric Shusta, University of Madison Wisconsin, Madison, USA; James McGrath, University of Rochester, NY, USA

Grants

- SNSF (310030E_189312; 310030_189080; 310030_189226; 4078PO_198297)
- NIH R61/R33, Fidelity Bermuda Foundation, EU Horizon 2020 ITN ENTRAIN, Swiss MS Society, Bern Center for Precision Medicine, CSL Behring
- UniBE ID grant (with Prof. Paola Luciani, DCB), Swiss Heart Foundation, Synapsis Foundation
- Scherbarth Foundation, Italian Multiple Sclerosis Foundation

Highlights



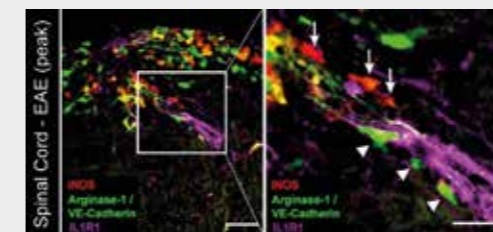
Decalcified mouse skull section showing outflow of fluorescent ovalbumin (OVA) into the nasal tissue lymphatics (LYVE-1+)

Drainage of cerebrospinal fluid (CSF) through the cribriform plate to nasopharyngeal lymphatics

In a collaborative project with researchers at the University of the Saarland, we have established an MRI assay to measure the dynamics of CSF flow after a low-rate infusion of contrast agent into the lateral ventricle of mice. This study demonstrated a rapid outflow of CSF along cranial nerves, especially along olfactory nerves to the nasal mucosa to reach lymphatic vessels draining this tissue. We validated this finding on decalcified sections after CSF injection of a fluorescent tracer Decker et al, 2021 <https://insight.jci.org/articles/view/150881>.

Cells of the blood brain barrier prime invading monocytes toward distinct inflammatory functions

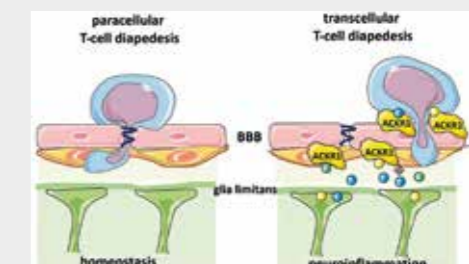
Our group has shown that monocytes trafficking to the central nervous system during autoimmune inflammation acquire distinct inflammatory features following interaction with endothelial cells of the blood brain barrier. In particular, we described an indirect role of the cytokine IL1 β in shaping anti-inflammatory functions of invading myeloid cells. Ivan et al., 2021, <https://doi.org/10.3389/fimmu.2021.666961>.



Differential polarization of macrophages in the mouse spinal cord during neuroinflammation

ACKR1 promotes transcellular T-cell diapedesis across the inflamed blood-brain barrier

Microvascular endothelial cells of the central nervous system (CNS) form the blood-brain barrier (BBB), which tightly regulates the migration of immune cells from the blood into the immune privileged CNS. Accounting for its barrier properties, multi-step T-cell migration across the BBB is characterized by unique adaptations. One of those is that T cell cross the inflamed BBB transcellular, through pores of BBB endothelial cells, rather than through the endothelial junctions. We could identify the atypical chemokine receptor 1 (ACKR1), expression of which is induced at the inflamed BBB, to mediate transcellular T-cell diapedesis across the inflamed BBB by shuttling inflammatory chemokines from the abluminal to the luminal side of the BBB. Marchetti et al., EJI, 2021, <https://doi.org/10.1002/eji.202149238>



ACKR1 is upregulated at the inflamed BBB and shuttles inflammatory chemokines from the abluminal to luminal BBB which increases transcellular T-cell diapedesis

3 PhD students could finalize their PhD thesis in 2021 at the TKI

Dr. Sidar Aydin, thesis title: "Cellular and molecular mechanisms involved in CD8+ T-cell migration across the blood-brain barrier during immunosurveillance and neuroinflammation", February 5th, 2021

Dr. Daniela Condescu-Ivan, thesis title: "Myeloid cell recruitment to the CNS during neuroinflammation – migration pathways and functional polarizations", August 4th, 2021

Dr. Federico Saltarin, thesis title: "Investigations on the extravasation of melanoma cells across the blood brain barrier", December 10th, 2021



Dr. Sidar Aydin



Dr. Daniela Ivan



Dr. Federico Saltarin