Curriculum Vitae Aurel Perren 26.4.2022

1. **Aurel Amos Perren**, born January 12th 1970 in Basel, Switzerland

Department of Pathology, Murtenstrasse 31, 3018 Bern, University of Bern
Email: aurel.perren@pathology.unibe.ch.
Phone: -41 31 632 32 23
ORCID: 0000-0002-6819-6092; Google Scholar ID: bIrBlFgAAAAJ

2. Education

1995:	Degree in Medicine, University of Basel, Switzerland
Nov 5th 1995:	State board examination (Staatsexamen)
1998:	University of Zürich, MD Thesis
2002 and 2004	Swiss board examination in Pathology and molecular Pathology
2005:	Lecturer degree (PD), University of Zürich

3. Employment history

1996 – 1998	Resident in Pathology and Surgery, UZH and Bruderholz
1998	Research fellow, Adult genetics Department, Dana Farber Cance Institute, Boston, USA
1999 – 2002	Resident, Department of Pathology, Liestal and Zürich, Switzerland
2002 – 2007	Staff member, Department of Pathology, University Hospital of Zürich
2007 - 2009	Professor for tumor pathology (W2), Institute for Pathology, Klinikum rechts der Isar, Technische Universität München, Germany
2009 -	Professor of Pathology and Director of the Institute of Pathology, University of Bern

4. Approved research projects

1998	Lydia Hochstrasser- Stiftung Zürich: „PTEN expression in breast cancer": PI: Sfr. 15´000
2002-2004	Pottère Stiftung Zürich: „Expression array analysis of pancreatic endocrine tumors": PI: SFr. 150'000.-
2005-2008	Schweizerischer Nationalfonds SNF Grant No. 31-108257: Genetik endokriner Pankreastumoren: Protein-, RNA- und Mutationsanalyse von Kandidatengenen: PI: SFr. 227'000.-
2012-2015	Schweizerischer Nationalfonds SNF Grant No. 310030_144236: "The role of Daxx in initiation and progression of pancreatic neuroendocrine tumors (pNET)": PI: SFr. 367'00.-
2014-2017	Schweizerische Krebsforschung Grant. "The role of autophagy in development of therapy resistance in pancreatic NET": PI: SFr. 257'000.-
2014-2019	SNF-Grant: Establishment of a "Swiss Biobanking Platform": PI: V. Moser, Co-PIs: T. Leeb, A. Perren and N Probst: SFr 3'200'000.-
2017-2020	SNF-Grant: "PathoLINK: Connecting biobanks to determine mechanisms of metastasis formation and chemoresistance": PI: H. Moch, Co-PI:, Perren: SFr 1'500'000.-
2018-2021	Schweizerische Krebsforschung Grant 4227-08-2017: " Precision medicine approach for novel epigenetic treatment for PanNET": SFr 359'450
2020-2021	UNISCIENCIA Stiftung : Epigenetic regulation in DAXX/ATRX negative Pancreatic Neuro-Endocrine Tumors (PanNET): PI: Aurel Perren, SFr 135'000.-
2020-2024	SNF-Grant (310030_188639) Metabolic changes in early and late progression steps of pancreatic neuroendocrine tumors: PI: Aurel Perren, SFr 632'000.-
2021-2024	PHRT-PIP: Towards holistic tissue analyses: a PIP for 3D non-invasive histopathology of thyroid tumors for precision medicine: PI: R. Zboray, EMPA

Major scientific achievements Prof. Aurel Perren

Biology of Pancreatic neuroendocrine tumors (PanNET)

My research work focuses since my doctoral thesis 1998 (clonal heterogeneity of pancreatic neuroendocrine tumors) on understanding, diagnosing and classifying PanNET, starting from human patient samples and questioning observations on human samples using *in-vitro* and *in-vivo* models.

To examine human NET tumor initiation, we used a detailed histological and molecular exam of precursor lesions in familial settings of NET as a human models for tumorigenesis. We demonstrated in duodenal NET of MEN1-patients that microscopic proliferations of G-cells were monoclonal and occurred multifocally in the duodenum in the background of a polyclonal G- cell hyperplasia. This observation explained the 100% relapse rate of MEN1-associated Gastrinomas after the Thompson procedure. In pancreatic resections of MEN1 patients we detected monohormonal endocrine cell clusters as smallest monoclonal form of PanNET. Such lesions as well as microadenomas are distributed all over the pancreas and explain clinical relapses, however it is unclear why only a very minute proportion of these early PanNET progresses. We could prove an islet origin of at least a subset of human PanNET by the presence of such early lesions in islets (SNF funded). Examining this morphological form of microadenomatosis, we could characterize two novel human diseases (Glucagon-cell adenomatosis and insulinomatosis), in the meanwhile, genomic analysis have confirmed a specific mutation as cause of the former.

Understanding PanNET progression from indolent early lesions to clinically malignant and metastasizing tumors is needed to define potential targets. In Zürich I contributed to conventional comparative genomic hybridization (CGH) and array CGH analyses that could demonstrate only few gross chromosomal aberrations in small (<2cm) PanNET and more than 8 such abrerrations in clinically malignant PanNET including insulinomas, which we defined as chromosomal instability. The molecular basis for this chromosomal instability remained unclear until our discovery, that DAXX/ATRX mutations do not only lead to the alternative lengthening of telomeres phenotype in a subset of PanNET, but also to chromosomal instability. This lead to the ongoing in-depth analysis of the role of epigenetic modifications in induction of malignancy and chromosomal instability, a project that is followed now by Dr. Ilaria Marinoni working as an independent researcher. In this project she describes epigenetically defined PanNET subtypes, indicating at least two different cells of origin and progression through accumulating epigenetic changes, driven by MEN1, DAXX and ATRX mutations.

In the framework of a KLS-funded project we discovered in mouse models that lysosomal instability is involved in PanNET response and resistance to Sunitinib treatment, which we could confirm in patient derived PanNET primary cell culture. The development of this 3D culture model allows to bridge the gap between highly proliferative PanNET cell lines (BON1, QGP1 and recently NT3) and human slowly proliferating tumors. This technology has the potential to be able to predict therapy response in humans and to test novel drugs, an approach we are currently following under a KLS- project testing novel epigenetic treatments based on the epigenetic results described. To overcome the rarity of the disease, national (PathoLINK) and international collaborations (Paris, Milan and Marburg) are running and these tumors are available for the primary cell-culture analysis.

Biobanking activities

As responsible of the Tissue biobank in the TU Munich and as member of the evaluation committee for the German BMBF initiative on central Biomaterial Banks (cBMB initiative) I became more aware of the central needs of coordinated and controlled biobanking activities. After arriving to Bern 2009, I did set-up with the Tissue Biobank Bern a HFG-conform tissue biobanking service in the Institute of Pathology, which has been awarded the Norma label by Swiss Biobanking Platform (SBP) and which is actually preparing accreditation according to SAS. For improving inter-institutional coordination in Switzerland, I lead the Working group 2 on tissue biobanking of the SNF-funded Swiss Biobanking Platform (SBP) implementing common minimal standards (SPREC), data structure to facilitate exchange of samples. As participant in the SNF-funded Patho-LINK project, I work on harmonizing Pathology reports in all five Swiss University Hospitals, as this will massively facilitate samples exchange in the future.